



Sequence Listing

<110> de Sauvage, Frederic
Carpenter, David A.

<120> Patched-2 Antibodies

<130> P1405R1C1

<140> US 09/293,505

<141> 1999-04-14

<150> US 60/081,884

<151> 1998-04-15

<160> 24

<210> 1

<211> 4030

<212> DNA

<213> Homo sapiens

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BEST AVAILABLE COPY

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<211> 1203

<212> PRT

<213> Homo sapiens

<400> 2

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				20					25					30	
Lys	Ala	Pro	Leu	Trp	Leu	Arg	Ala	Tyr	Phe	Gln	Gly	Leu	Leu	Phe	
				35					40					45	
Ser	Leu	Gly	Cys	Gly	Ile	Gln	Arg	His	Cys	Gly	Lys	Val	Leu	Phe	
				50					55					60	
Leu	Gly	Leu	Leu	Ala	Phe	Gly	Ala	Leu	Ala	Leu	Gly	Leu	Arg	Met	
				65					70					75	
Ala	Ile	Ile	Glu	Thr	Asn	Leu	Glu	Gln	Leu	Trp	Val	Glu	Val	Gly	
				80					85					90	
Ser	Arg	Val	Ser	Gln	Glu	Leu	His	Tyr	Thr	Lys	Glu	Lys	Leu	Gly	
				95					100					105	
Glu	Glu	Ala	Ala	Tyr	Thr	Ser	Gln	Met	Leu	Ile	Gln	Thr	Ala	Arg	
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Gln	Glu	Gly	Glu	Asn	Ile	Leu	Thr	Pro	Glu	Ala	Leu	Gly	Leu	His	
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Leu	Gln	Ala	Ala	Leu	Thr	Ala	Ser	Lys	Val	Gln	Val	Ser	Leu	Tyr	
				140					145					150	
Gly	Lys	Ser	Trp	Asp	Leu	Asn	Lys	Ile	Cys	Tyr	Lys	Ser	Gly	Val	
				155					160					165	
Pro	Leu	Ile	Glu	Asn	Gly	Met	Ile	Glu	Trp	Met	Ile	Glu	Lys	Leu	
				170					175					180	
Phe	Pro	Cys	Val	Ile	Leu	Thr	Pro	Leu	Asp	Cys	Phe	Trp	Glu	Gly	
				185					190					195	
Ala	Lys	Leu	Gln	Gly	Gly	Ser	Ala	Tyr	Leu	Pro	Gly	Arg	Pro	Asp	
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Ile	Gln	Trp	Thr	Asn	Leu	Asp	Pro	Glu	Gln	Leu	Leu	Glu	Glu	Leu	
				215					220					225	
Gly	Pro	Phe	Ala	Ser	Leu	Glu	Gly	Phe	Arg	Glu	Leu	Leu	Asp	Lys	
				230					235					240	
Ala	Gln	Val	Gly	Gln	Ala	Tyr	Val	Gly	Arg	Pro	Cys	Leu	His	Pro	
				245					250					255	
Asp	Asp	Leu	His	Cys	Pro	Pro	Ser	Ala	Pro	Asn	His	His	Ser	Arg	
				260					265					270	

Gln Ala Pro Asn Val Ala His Glu Leu Ser Gly Gly Cys His Gly	275	280	285
Phe Ser His Lys Phe Met His Trp Gln Glu Glu Leu Leu Leu Gly	290	295	300
Gly Met Ala Arg Asp Pro Gln Gly Glu Leu Leu Arg Ala Glu Ala	305	310	315
Leu Gln Ser Thr Phe Leu Leu Met Ser Pro Arg Gln Leu Tyr Glu	320	325	330
His Phe Arg Gly Asp Tyr Gln Thr His Asp Ile Gly Trp Ser Glu	335	340	345
Glu Gln Ala Ser Thr Val Leu Gln Ala Trp Gln Arg Arg Phe Val	350	355	360
Gln Leu Ala Gln Glu Ala Leu Pro Glu Asn Ala Ser Gln Gln Ile	365	370	375
His Ala Phe Ser Ser Thr Thr Leu Asp Asp Ile Leu His Ala Phe	380	385	390
Ser Glu Val Ser Ala Ala Arg Val Val Gly Gly Tyr Leu Leu Met	395	400	405
Leu Ala Tyr Ala Cys Val Thr Met Leu Arg Trp Asp Cys Ala Gln	410	415	420
Ser Gln Gly Ser Val Gly Leu Ala Gly Val Leu Leu Val Ala Leu	425	430	435
Ala Val Ala Ser Gly Leu Gly Leu Cys Ala Leu Leu Gly Ile Thr	440	445	450
Phe Asn Ala Ala Thr Thr Gln Val Leu Pro Phe Leu Ala Leu Gly	455	460	465
Ile Gly Val Asp Asp Val Phe Leu Leu Ala His Ala Phe Thr Glu	470	475	480
Ala Leu Pro Gly Thr Pro Leu Gln Glu Arg Met Gly Glu Cys Leu	485	490	495
Gln Arg Thr Gly Thr Ser Val Val Leu Thr Ser Ile Asn Asn Met	500	505	510
Ala Ala Phe Leu Met Ala Ala Leu Val Pro Ile Pro Ala Leu Arg	515	520	525
Ala Phe Ser Leu Gln Ala Ala Ile Val Val Gly Cys Thr Phe Val	530	535	540
Ala Val Met Leu Val Phe Pro Ala Ile Leu Ser Leu Asp Leu Arg	545	550	555
Arg Arg His Cys Gln Arg Leu Asp Val Leu Cys Cys Phe Ser Ser	560	565	570

Pro Cys Ser Ala Gln Val Ile Gln Ile Leu Pro Gln Glu Leu Gly	575	580	585
Asp Gly Thr Val Pro Val Gly Ile Ala His Leu Thr Ala Thr Val	590	595	600
Gln Ala Phe Thr His Cys Glu Ala Ser Ser Gln His Val Val Thr	605	610	615
Ile Leu Pro Pro Gln Ala His Leu Val Pro Pro Pro Ser Asp Pro	620	625	630
Leu Gly Ser Glu Leu Phe Ser Pro Gly Gly Ser Thr Arg Asp Leu	635	640	645
Leu Gly Gln Glu Glu Glu Thr Arg Gln Lys Ala Ala Cys Lys Ser	650	655	660
Leu Pro Cys Ala Arg Trp Asn Leu Ala His Phe Ala Arg Tyr Gln	665	670	675
Phe Ala Pro Leu Leu Leu Gln Ser His Ala Lys Ala Ile Val Leu	680	685	690
Val Leu Phe Gly Ala Leu Leu Gly Leu Ser Leu Tyr Gly Ala Thr	695	700	705
Leu Val Gln Asp Gly Leu Ala Leu Thr Asp Val Val Pro Arg Gly	710	715	720
Thr Lys Glu His Ala Phe Leu Ser Ala Gln Leu Arg Tyr Phe Ser	725	730	735
Leu Tyr Glu Val Ala Leu Val Thr Gln Gly Gly Phe Asp Tyr Ala	740	745	750
His Ser Gln Arg Ala Leu Phe Asp Leu His Gln Arg Phe Ser Ser	755	760	765
Leu Lys Ala Val Leu Pro Pro Pro Ala Thr Gln Ala Pro Arg Thr	770	775	780
Trp Leu His Tyr Tyr Arg Asn Trp Leu Gln Gly Ile Gln Ala Ala	785	790	795
Phe Asp Gln Asp Trp Ala Ser Gly Arg Ile Thr Arg His Ser Tyr	800	805	810
Arg Asn Gly Ser Glu Asp Gly Ala Leu Ala Tyr Lys Leu Leu Ile	815	820	825
Gln Thr Gly Asp Ala Gln Glu Pro Leu Asp Phe Ser Gln Leu Thr	830	835	840
Thr Arg Lys Leu Val Asp Arg Glu Gly Leu Ile Pro Pro Glu Leu	845	850	855
Phe Tyr Met Gly Leu Thr Val Trp Val Ser Ser Asp Pro Leu Gly	860	865	870
Leu Ala Ala Ser Gln Ala Asn Phe Tyr Pro Pro Pro Pro Glu Trp			

875	880	885
Leu His Asp Lys Tyr Asp Thr Thr Gly Glu Asn Leu Arg Ile Pro		
890	895	900
Pro Ala Gln Pro Leu Glu Phe Ala Gln Phe Pro Phe Leu Leu Arg		
905	910	915
Gly Leu Gln Lys Thr Ala Asp Phe Val Glu Ala Ile Glu Gly Ala		
920	925	930
Arg Ala Ala Cys Ala Glu Ala Gly Gln Ala Gly Val His Ala Tyr		
935	940	945
Pro Ser Gly Ser Pro Phe Leu Phe Trp Glu Gln Tyr Leu Gly Leu		
950	955	960
Arg Arg Cys Phe Leu Leu Ala Val Cys Ile Leu Leu Val Cys Thr		
965	970	975
Phe Leu Val Cys Ala Leu Leu Leu Leu Asn Pro Trp Thr Ala Gly		
980	985	990
Leu Ile Val Leu Val Leu Ala Met Met Thr Val Glu Leu Phe Gly		
995	1000	1005
Ile Met Gly Phe Leu Gly Ile Lys Leu Ser Ala Ile Pro Val Val		
1010	1015	1020
Ile Leu Val Ala Ser Val Gly Ile Gly Val Glu Phe Thr Val His		
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Val Ala Leu Gly Phe Leu Thr Thr Gln Gly Ser Arg Asn Leu Arg		
1040	1045	1050
Ala Ala His Ala Leu Glu His Thr Phe Ala Pro Val Thr Asp Gly		
1055	1060	1065
Ala Ile Ser Thr Leu Leu Gly Leu Leu Met Leu Ala Gly Ser His		
1070	1075	1080
Phe Asp Phe Ile Val Arg Tyr Phe Phe Ala Ala Leu Thr Val Leu		
1085	1090	1095
Thr Leu Leu Gly Leu Leu His Gly Leu Val Leu Leu Pro Val Leu		
1100	1105	1110
Leu Ser Ile Leu Gly Pro Pro Pro Glu Val Ile Gln Met Tyr Lys		
1115	1120	1125
Glu Ser Pro Glu Ile Leu Ser Pro Pro Ala Pro Gln Gly Gly Gly		
1130	1135	1140
Leu Arg Trp Gly Ala Ser Ser Ser Leu Pro Gln Ser Phe Ala Arg		
1145	1150	1155
Val Thr Thr Ser Met Thr Val Ala Ile His Pro Pro Pro Leu Pro		
1160	1165	1170
Gly Ala Tyr Ile His Pro Ala Pro Asp Glu Pro Pro Trp Ser Pro		
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Ala Ala Thr Ser Ser Gly Asn Leu Ser Ser Arg Gly Pro Gly Pro
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Ala Thr Gly

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<212> DNA
<213> Homo sapiens

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<222> 20, 27, 135, 156, 210
<223> unknown base

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ggcctnatag tgctggctct ggcgatgatg acagtggaaac tctttggtat 200
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<211> 153
<212> DNA
<213> Homo sapiens

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<222> 143
<223> Unknown base

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tct 153

<210> 5
<211> 228
<212> DNA
<213> Homo sapiens

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gatgggcctc atcggaatca agctcagt 228

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<211> 50
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> 13-14
<223> unknown base

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<210> 7
<211> 1397
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35 40 45
Asp Arg Asp Tyr Leu His Arg Pro Ser Tyr Cys Asp Ala Ala Phe
50 55 60
Ala Leu Glu Gln Ile Ser Lys Gly Lys Ala Thr Gly Arg Lys Ala
65 70 75
Pro Leu Trp Leu Arg Ala Lys Phe Gln Arg Leu Leu Phe Lys Leu
80 85 90
Gly Cys Tyr Ile Gln Lys Asn Cys Gly Lys Ala Met Phe Asn Pro
95 100 105
Gln Leu Met Ile Gln Thr Pro Lys Glu Glu Gly Ala Asn Val Leu
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Thr Thr Glu Ala Leu Leu Gln His Leu Asp Ser Ala Leu Gln Ala
125 130 135
Ser Arg Val His Val Tyr Met Tyr Asn Arg Gln Trp Lys Leu Glu
140 145 150
His Leu Cys Tyr Lys Ser Gly Glu Leu Ile Thr Glu Thr Gly Tyr
155 160 165
Met Asp Gln Ile Ile Glu Tyr Leu Tyr Pro Cys Leu Ile Ile Thr
170 175 180
Pro Leu Asp Cys Phe Trp Glu Gly Ala Lys Leu Gln Ser Gly Thr
185 190 195
Ala Tyr Leu Leu Gly Lys Pro Pro Leu Arg Trp Thr Asn Phe Asp

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Pro Leu Glu Phe	Leu Glu Glu Leu Lys	Lys Ile Asn Tyr Gln	Val
	215	220	225
Asp Ser Trp Glu	Glu Met Leu Asn Lys	Ala Glu Val Gly His	Gly
	230	235	240
Tyr Met Asp Arg	Pro Cys Leu Asn Pro	Ala Asp Pro Asp Cys	Pro
	245	250	255
Ala Thr Ala Pro	Asn Lys Asn Ser Thr	Lys Pro Leu Asp Met	Ala
	260	265	270
Leu Val Leu Asn	Gly Gly Cys His Gly	Leu Ser Arg Lys Tyr	Met
	275	280	285
His Trp Gln Glu	Glu Leu Ile Val Gly	Gly Thr Val Lys Asn	Ser
	290	295	300
Thr Gly Lys Leu	Val Ser Ala His Ala	Leu Gln Thr Met Phe	Gln
	305	310	315
Leu Met Thr Pro	Lys Gln Met Tyr Glu	His Phe Lys Gly Tyr	Glu
	320	325	330
Tyr Val Ser His	Ile Asn Trp Asn Glu	Asp Lys Ala Ala Ala	Ile
	335	340	345
Leu Glu Ala Trp	Gln Arg Thr Tyr Val	Glu Val Val His Gln	Ser
	350	355	360
Val Ala Gln Asn	Ser Thr Gln Lys Val	Leu Ser Phe Thr Thr	Thr
	365	370	375
Thr Leu Asp Asp	Ile Leu Lys Ser Phe	Ser Asp Val Ser Val	Ile
	380	385	390
Arg Val Ala Ser	Gly Tyr Leu Leu Met	Leu Ala Tyr Ala Cys	Leu
	395	400	405
Thr Met Leu Arg	Trp Asp Cys Ser Lys	Ser Gln Gly Ala Val	Gly
	410	415	420
Leu Ala Gly Val	Leu Leu Val Ala Leu	Ser Val Ala Ala Gly	Leu
	425	430	435
Gly Leu Cys Ser	Leu Ile Gly Ile Ser	Phe Asn Ala Ala Thr	Thr
	440	445	450
Gln Val Leu Pro	Phe Leu Ala Leu Gly	Val Gly Val Asp Asp	Val
	455	460	465
Phe Leu Leu Ala	His Ala Phe Ser Glu	Thr Gly Gln Asn Lys	Arg
	470	475	480
Ile Pro Phe Glu	Asp Arg Thr Gly Glu	Cys Leu Lys Arg Thr	Gly
	485	490	495
Ala Ser Val Ala	Leu Thr Ser Ile Ser	Asn Val Thr Ala Phe	Phe
	500	505	510

Met	Ala	Ala	Leu	Ile	Pro	Ile	Pro	Ala	Leu	Arg	Ala	Phe	Ser	Leu			
				515					520					525			
Gln	Ala	Ala	Val	Val	Val	Val	Phe	Asn	Phe	Ala	Met	Val	Leu	Leu			
				530					535					540			
Ile	Phe	Pro	Ala	Ile	Leu	Ser	Met	Asp	Leu	Tyr	Arg	Arg	Glu	Asp			
				545					550					555			
Arg	Arg	Leu	Asp	Ile	Phe	Cys	Cys	Phe	Thr	Ser	Pro	Cys	Val	Ser			
				560					565					570			
Arg	Val	Ile	Gln	Val	Glu	Pro	Gln	Ala	Tyr	Thr	Asp	Thr	His	Asp			
				575					580					585			
Asn	Thr	Arg	Tyr	Ser	Pro	Pro	Pro	Pro	Tyr	Ser	Ser	His	Ser	Phe			
				590					595					600			
Ala	His	Glu	Thr	Gln	Ile	Thr	Met	Gln	Ser	Thr	Val	Gln	Leu	Arg			
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Thr	Glu	Tyr	Asp	Pro	His	Thr	His	Val	Tyr	Tyr	Thr	Thr	Ala	Glu			
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Pro	Arg	Ser	Glu	Ile	Ser	Val	Gln	Pro	Val	Thr	Val	Thr	Gln	Asp			
				635					640					645			
Thr	Leu	Ser	Cys	Gln	Ser	Pro	Glu	Ser	Thr	Ser	Ser	Thr	Arg	Asp			
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Leu	Leu	Ser	Gln	Phe	Ser	Asp	Ser	Ser	Leu	His	Cys	Leu	Glu	Pro			
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Ala	Pro	Phe	Leu	Leu	Lys	Pro	Lys	Ala	Lys	Val	Val	Val	Ile	Phe			
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Leu	Phe	Leu	Gly	Leu	Leu	Gly	Val	Ser	Leu	Tyr	Gly	Thr	Thr	Arg			
				710					715					720			
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Arg	Glu	Tyr	Asp	Phe	Ile	Ala	Ala	Gln	Phe	Lys	Tyr	Phe	Ser	Phe			
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Tyr	Asn	Met	Tyr	Ile	Val	Thr	Gln	Lys	Ala	Asp	Tyr	Pro	Asn	Ile			
				755					760					765			
Gln	His	Leu	Leu	Tyr	Asp	Leu	His	Arg	Ser	Phe	Ser	Asn	Val	Lys			
				770					775					780			
Tyr	Val	Met	Leu	Glu	Glu	Asn	Lys	Gln	Leu	Pro	Lys	Met	Trp	Leu			
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His	Tyr	Phe	Arg	Asp	Trp	Leu	Gln	Gly	Leu	Gln	Asp	Ala	Phe	Asp			
				800					805					810			

Ser Asp Trp Glu Thr Gly Lys Ile Met Pro Asn Asn Tyr Lys Asn	815	820	825
Gly Ser Asp Asp Gly Val Leu Ala Tyr Lys Leu Leu Val Gln Thr	830	835	840
Gly Ser Arg Asp Lys Pro Ile Asp Ile Ser Gln Leu Thr Lys Gln	845	850	855
Arg Leu Val Asp Ala Asp Gly Ile Ile Asn Pro Ser Ala Phe Tyr	860	865	870
Ile Tyr Leu Thr Ala Trp Val Ser Asn Asp Pro Val Ala Tyr Ala	875	880	885
Ala Ser Gln Ala Asn Ile Arg Pro His Arg Pro Glu Trp Val His	890	895	900
Asp Lys Ala Asp Tyr Met Pro Glu Thr Arg Leu Arg Ile Pro Ala	905	910	915
Ala Glu Pro Ile Glu Tyr Ala Gln Phe Pro Phe Tyr Leu Asn Gly	920	925	930
Leu Arg Asp Thr Ser Asp Phe Val Glu Ala Ile Glu Lys Val Arg	935	940	945
Thr Ile Cys Ser Asn Tyr Thr Ser Leu Gly Leu Ser Ser Tyr Pro	950	955	960
Asn Gly Tyr Pro Phe Leu Phe Trp Glu Gln Tyr Ile Gly Leu Arg	965	970	975
His Trp Leu Leu Leu Phe Ile Ser Val Val Leu Ala Cys Thr Phe	980	985	990
Leu Val Cys Ala Val Phe Leu Leu Asn Pro Trp Thr Ala Gly Ile	995	1000	1005
Ile Val Met Val Leu Ala Leu Met Thr Val Glu Leu Phe Gly Met	1010	1015	1020
Met Gly Leu Ile Gly Ile Lys Leu Ser Ala Val Pro Val Val Ile	1025	1030	1035
Leu Ile Ala Ser Val Gly Ile Gly Val Glu Phe Thr Val His Val	1040	1045	1050
Ala Leu Ala Phe Leu Thr Ala Ile Gly Asp Lys Asn Arg Arg Ala	1055	1060	1065
Val Leu Ala Leu Glu His Met Phe Ala Pro Val Leu Asp Gly Ala	1070	1075	1080
Val Ser Thr Leu Leu Gly Val Leu Met Leu Ala Gly Ser Glu Phe	1085	1090	1095
Asp Phe Ile Val Arg Tyr Phe Phe Ala Val Leu Ala Ile Leu Thr	1100	1105	1110
Ile Leu Gly Val Leu Asn Gly Leu Val Leu Leu Pro Val Leu Leu			

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Asn Arg Leu Pro Thr Pro Ser Pro Glu Pro Pro Pro Ser Val Val		
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Arg Phe Ala Met Pro Pro Gly His Thr His Ser Gly Ser Asp Ser		
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Ser Asp Ser Glu Tyr Ser Ser Gln Thr Thr Val Ser Gly Leu Ser		
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Glu Glu Leu Arg His Tyr Glu Ala Gln Gln Gly Ala Gly Gly Pro		
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His Ser Thr Val Val His Pro Glu Ser Arg His His Pro Pro Ser		
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Asn Pro Arg Gln Gln Pro His Leu Asp Ser Gly Ser Leu Pro Pro		
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Gly Arg Gln Gly Gln Gln Pro Arg Arg Asp Pro Pro Arg Glu Gly		
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Leu Trp Pro Pro Leu Tyr Arg Pro Arg Arg Asp Ala Phe Glu Ile		
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Ser Thr Glu Gly His Ser Gly Pro Ser Asn Arg Ala Arg Trp Gly		
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Pro Arg Gly Ala Arg Ser His Asn Pro Arg Asn Pro Ala Ser Thr		
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Ala Met Gly Ser Ser Val Pro Gly Tyr Cys Gln Pro Ile Thr Thr		
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Val Thr Ala Ser Ala Ser Val Thr Val Ala Val His Pro Pro Pro		
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Val Pro Gly Pro Gly Arg Asn Pro Arg Gly Gly Leu Cys Pro Gly		
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Tyr Pro Glu Thr Asp His Gly Leu Phe Glu Asp Pro His Val Pro		
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Phe His Val Arg Cys Glu Arg Arg Asp Ser Lys Val Glu Val Ile		
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Glu Leu Gln Asp Val Glu Cys Glu Glu Arg Pro Arg Gly Ser Ser		
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Ser Asn		

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<211> 1182

<212> PRT

<213> Mus musculus

<400> 8

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Gln	Ala	Pro	Leu	Trp	Leu	Arg	Ala	Tyr	Phe	Gln	Gly	Leu	Leu	Phe	
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Leu	Gly	Leu	Val	Ala	Phe	Gly	Ala	Leu	Ala	Leu	Gly	Leu	Arg	Val	
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Phe	Pro	Cys	Val	Ile	Leu	Thr	Pro	Leu	Asp	Cys	Phe	Trp	Glu	Gly	
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Ala	Lys	Leu	Gln	Gly	Gly	Ser	Ala	Tyr	Leu	Pro	Gly	Arg	Pro	Asp	
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Gln	Ala	Pro	Asn	Val	Ala	Gln	Glu	Leu	Ser	Gly	Gly	Cys	His	Gly	
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Gly Thr Ala Arg	Asp Leu Gln Gly Gln	Leu Leu Arg Ala Glu	Ala
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Leu Gln Ser Thr	Phe Leu Leu Met Ser	Pro Arg Gln Leu Tyr	Glu
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His Phe Arg Gly	Asp Tyr Gln Thr His	Asp Ile Gly Trp Ser	Glu
335	340		345
Glu Gln Ala Ser	Met Val Leu Gln Ala	Trp Gln Arg Arg Phe	Val
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Gln Leu Ala Gln	Glu Ala Leu Pro Ala	Asn Ala Ser Gln Gln	Ile
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His Ala Phe Ser	Ser Thr Thr Leu Asp	Asp Ile Leu Arg Ala	Phe
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Ser Glu Val Ser	Thr Thr Arg Val Val	Gly Gly Tyr Leu Leu	Met
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Leu Ala Tyr Ala	Cys Val Thr Met Leu	Arg Trp Asp Cys Ala	Gln
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Ser Gln Gly Ala	Val Gly Leu Ala Gly	Val Leu Leu Val Ala	Leu
425	430		435
Ala Val Ala Ser	Gly Leu Gly Leu Cys	Ala Leu Leu Gly Ile	Thr
440	445		450
Phe Asn Ala Ala	Thr Thr Gln Val Leu	Pro Phe Leu Ala Leu	Gly
455	460		465
Ile Gly Val Asp	Asp Ile Phe Leu Leu	Ala His Ala Phe Thr	Lys
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485	490		495
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Val Ala Phe Phe	Met Ala Ala Leu Val	Pro Ile Pro Ala Leu	Arg
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Ala Phe Ser Leu	Gln Ala Ala Ile Val	Val Gly Cys Asn Phe	Ala
530	535		540
Ala Val Met Leu	Val Phe Pro Ala Ile	Leu Ser Leu Asp Leu	Arg
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Arg Arg His Arg	Gln Arg Leu Asp Val	Leu Cys Cys Phe Ser	Ser
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Pro Cys Ser Ala	Gln Val Ile Gln Met	Leu Pro Gln Glu Leu	Gly
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Leu Ser Gln Glu Glu Gly Thr Gly Pro Gln Ala Ala Cys Arg Pro		
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Leu Leu Cys Ala His Trp Thr Leu Ala His Phe Ala Arg Tyr Gln		
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Phe Ala Pro Leu Leu Leu Gln Thr Arg Ala Lys Ala Leu Val Leu		
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Leu Tyr Glu Val Ala Leu Val Thr Gln Gly Gly Phe Asp Tyr Ala		
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His Ser Gln Arg Ala Leu Phe Asp Leu His Gln Arg Phe Ser Ser		
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Gln Thr Gly Asn Ala Gln Glu Pro Leu Asp Phe Ser Gln Leu Thr		
830	835	840
Thr Arg Lys Leu Val Asp Lys Glu Gly Leu Ile Pro Pro Glu Leu		
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Phe Tyr Met Gly Leu Thr Val Trp Val Ser Ser Asp Pro Leu Gly		
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875	880	885
Leu His Asp Lys Tyr Asp Thr Thr Gly Glu Asn Leu Arg Ile Pro		
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Gly Leu Gln Lys Thr Ala Asp Phe Val Glu Ala Ile Glu Gly Ala	920	925	930
Arg Ala Ala Cys Thr Glu Ala Gly Gln Ala Gly Val His Ala Tyr	935	940	945
Pro Ser Gly Ser Pro Phe Leu Phe Trp Glu Gln Tyr Leu Gly Leu	950	955	960
Arg Arg Cys Phe Leu Leu Ala Val Cys Ile Leu Leu Val Cys Thr	965	970	975
Phe Leu Val Cys Ala Leu Leu Leu Leu Ser Pro Trp Thr Ala Gly	980	985	990
Leu Ile Val Leu Val Leu Ala Met Met Thr Val Glu Leu Phe Gly	995	1000	1005
Ile Met Gly Phe Leu Gly Ile Lys Leu Ser Ala Ile Pro Val Val	1010	1015	1020
Ile Leu Val Ala Ser Ile Gly Ile Gly Val Glu Phe Thr Val His	1025	1030	1035
Val Ala Leu Gly Phe Leu Thr Ser His Gly Ser Arg Asn Leu Arg	1040	1045	1050
Ala Ala Ser Ala Leu Glu Gln Thr Phe Ala Pro Val Thr Asp Gly	1055	1060	1065
Ala Val Ser Thr Leu Leu Gly Leu Leu Met Leu Ala Gly Ser Asn	1070	1075	1080
Phe Asp Phe Ile Ile Arg Tyr Phe Phe Val Val Leu Thr Val Leu	1085	1090	1095
Thr Leu Leu Gly Leu Leu His Gly Leu Leu Leu Leu Pro Val Leu	1100	1105	1110
Leu Ser Ile Leu Gly Pro Pro Pro Gln Val Val Gln Val Tyr Lys	1115	1120	1125
Glu Ser Pro Gln Thr Leu Asn Ser Ala Ala Pro Gln Arg Gly Gly	1130	1135	1140
Leu Arg Trp Asp Arg Pro Pro Thr Leu Pro Gln Ser Phe Ala Arg	1145	1150	1155
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<211> 4004

<212> DNA

<213> Homo sapiens

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<212> DNA

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<212> DNA
<213> Artificial Sequence
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<210> 19
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<213> Artificial Sequence
<220>
<223> sequence is synthesized

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<210> 21
<211> 48
<212> DNA
<213> Artificial Sequence
<220>
<223> sequence is synthesized

<400> 21

ggattctaatt acgactcact atagggcccc taaactccgc tgctccac 48

<210> 22

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<212> DNA

<213> Artificial Sequence

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<223> sequence is synthesized

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<212> DNA

<213> Artificial Sequence

<220>

<223> sequence is synthesized

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<210> 24

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<212> DNA

<213> Artificial Sequence

<220>

<223> sequence is synthesized

<400> 24

tcgacaagca gggaagtggg aagtagaagc tc 32



1 / 29

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 CAATAAAGTC CGGTACCACA ACGCGGCTTA ATTAAGGCT AGGTCTGTAC TATTCTATGT AACTACTCAA ACCTGTTTGG TGTGATCTT ACGTCACTTT

101 AAAATGCTTT ATTGTGAAA TTTGTGATGC TATTGCTTTA TTTGTAACCA TTATAAGCTG CAATAAACAA GTTGGGCCAT GCGGSCAAG CTTCTGCAGG
 TTTTACGAAA TAAACACTTT AAACACTAGC ATAACGAAAT AAACATTGGT AATATTCGAC GTTATTTGTT CAACCCGGTA CCGCCGGTTC GAAGACGTCC

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 AGCTGAGATC TCCTAGGGGC CCCTTAAGGC CGTACTGAGC TAGCGGCGGG GAGTCTCTCG ACGGGGCTC AATGTGTGGG GGTGAGACTT GCGTCTGTGG

1 M T R S P P L R E L P P S Y T P P A R T A A P

301 CCAGATCTTA GCTGGGAGCC TGAAGGCTCC ACTCTGGCTT CGTGCTTACT TCCAGGGCCT GCTCTCTCTCT CTGGGATGCG GGATCCAGAG ACATTGTGGC
 GGTCTAGGAT CGACCCCTCG ACTTCCGAGG TGAGACCGAA GCACGAATGA AGTCCCGGA CGAGAAGAGA GACCCCTACGC CCTAGGTCTC TGTAACACCG

24 Q I L A G S L K A P L W L R A Y F Q G L L F S L G C G I Q R H C G

401 AAAGTGTCT TTCTGGGACT GTTGGCCTTT GGGGCCCTGG CATTAGTCT CCGCATGGCC ATTATTGAGA CAAACTTGA ACAGCTCTGG GTAGAAGTGG
 TTTACAGAGA AAGACCCTGA CAACCGGAAA CCCCCGGACC GTAATCCAGA GCGTACCGG TAATAACTCT GTTTGAACCT TGTCGAGAGC CATCTTCACC

57 K V L F L G L L A F G A L A L G L R M A I I E T N L E Q L W V E V G

501 GCAGCCGGGT GAGCCAGGAG CTGCATTACA CCAAGGAGAA GCTGGGGGAG GAGGCTGCAT ACACCTCTCA GATGCTGATA CAGACCGCAC GCCAGGAGGG
 CTGCGGCCCCA CTCGGTCTTC GACGTAATGT GGTTCCTCTT CGACCCCTTC CTCCGACGTA TGTGGAGAGT CTACGACTAT GTCTGGCGTG CCGTCTCTCC

91 S R V S Q E L H Y T K E K L G E E A A Y T S Q M L I Q T A R Q E G

601 AGAGAACATC CTCACACCCG AAGCACTTGG CCTCCACCTC CAGGCAGCCC TCACTGCCAG TAAAGTCCAA GTATCACTCT ATGGGAAGTC CTGGGATTTG
 TCTCTGTAG GAGTGTGGC TTCGTGAACC GGAGGTGGAG GTCCGTCCGG AGTGACGGTC ATTTCAAGTT CAFAGTGAGA TACCCCTCAG GACCCTAAC

124 E N I L T P E A L G L H L Q A A L T A S K V Q V S L Y G K S W D L

701 AACAAAATCT GCTACAAGTC AGGAGTTCCC CTTATTGAAA ATGGAATGAT TGAGTGGATG ATTGAGAAGC TGTTCCTGTC CGTGATCCTC ACCCCCCCTCG
 TTGTTTGA CGATGTTTCA TCCTCAAGGG GAATAACTTT TACCTTACTA ACTCACCTAC TAACCTCTCG ACAAGGCAC GCACCTAGGAG TGGGGGAGC

157 N K I C Y K S G V P L I E N G M I E W M I E K L F P C V I L T P L D

FIG. 1A

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801 ACTGCTTCTG GGAGGGAGCC AAACCTCCAAG GGGGCTCCGC CTACCTGCCG GCGCGCCCGG ATATCCAGTG GACCAACCTG GATCCAGAGC AGCTGCTGGA
 TGACGAAGAC CCTCCCTCGG TTTGAGGTTT CCCCAGGCG GATGGACGGG CCGCGGGGCC TATAGGTCAC CTGGTTGGAC CTAGGTCTCG TCGACGACCT
 191 C F W E G A K L Q G G S A Y L P G R P D I Q W T N L D P E Q L L E
 901 GGAGCTGGGT CCCTTGCTT CCCTTGAGGG CTTCGGGAG CTGCTAGACA AGGCACAGGT GGGCCAGGCC TACGTGGGGC GGCCCTGTCT GCACCCCTGAT
 CCTCGACCCA GGGAACCGA GGGAACCTCC GAAGCCCTC GACGATCTGT TCCGTGTCCA CCGGTCCGG ATGCACCCCG CCGGGACAGA CGTGGGACTA
 224 E L G P F A S L E G F R E L L D K A Q V G Q A Y V G R P C L H P D
 1001 GACCTCCACT GCCCACCTAG TGCCCCCAAC CATCACAGCA GGCAGGCTCC CAATGTGGCT CACGAGCTGA GTGGGGGCTG CCATGGCTTC TCCACAAAT
 CTGGAGGTGA CCGGTGGATC ACGGGGGTTG GTAGTGTCTG CCGTCCGAGG GTTACACCGA GTGCTCGACT CACCCCGGAC GGTACCGAAG AGGGTGTGTA
 257 D L H C P P S A P N H H S R Q A P N V A H E L S G G C H G F S H K F
 1101 TCATGCACTG GCAGGAGGAA TTGCTGCTGG GAGGCATGCC CAGAGACCCC CAGGAGAGC TGCTGAGGC AGAGGCCCTG CAGAGCACCT TCTTGCTGAT
 AGTACGTGAC CGTCCTCCTT AACGAGGACC CTCCGTACCG GTCTCTGGG GTTCCTCTCG ACGACTCCG TCTCCGGGAC GTCTGCTGGA AGAAGGACTA
 291 M H W Q E E L L L G G M A R D P Q G E L L R A E A L Q S T F L L M
 1201 GAGTCCCCG CAGCTGTACG AGCATTTCCG GGGTGACTAT CAGACACATG ACATTTGGCTG GAGTGAGGAG CAGGCCAGCA CAGTGCTACA AGCCTGGCAG
 CTCAGGGCG GTGACATGC TCGTAAAGG CCCACTGATA GTCTGTGTAC TGTAACCGAC CTCACTCCTC GTCCGGTCTG GTCACGATGT TCGGACCGTC
 324 S P R Q L Y E H F R G D Y Q T H D I G W S E E Q A S T V L Q A W Q
 1301 CCGCGCTTG TGCAGCTGC CCAGGAGGCC CTGCCCTGAGA ACGTTCCCA GCAGATCCAT GCCTTCTCCT CCACCACCT GGATGACATC CTGCATGCGT
 GCGCGAAAC ACGTCGACCG GGTCTCTCCG GACGACTCT TCGGAAGGT CGTCTAGGTA CGGAAGAGGA GGTGTGGGA CCTACTGTAG GACGTACGCA
 357 R R F V Q L A Q E A L P E N A S Q Q I H A F S S T T L D D I L H A F
 1401 TCTCTGAAGT CAGTGCTGCC CGTGTGGTGG GAGGCTATCT GCTCATGCTG GCCTATGCCT GTGTGACCAT GCTGCGGTGG GACTGCGGCC AGTCCCAGGG
 AGAGACTTCA GTCACGACGG GCACACCACC CTCGATAGA CGAGTAGGAC CGGATACGGA CACACTGGTA CGAGCCACC CTGACGCGGG TCAGGTGCC
 391 S E V S A A R V V G G Y L L M L A Y A C V T M L R W D C A Q S Q G
 1501 TTCCGTGGC CTGCGCGGG TACTGCTGTT GGCCTGGCG GTGGCTCAG GCCTTGGCT CTGTGCCCTG CTGGCATCA CCTTCAATGC TGCCACTACC
 AAGGACCCG GAACGGCCCC ATGACGACCA CCGGACCG CACCGAGTC CGGAACCGA GACACGGGAC GAGCCGTAGT GGAAGTTACG ACGGTGATGG
 424 S V G L A G V L L V A L A V A S G L G L C A L L G I T F N A A T T

FIG. 1B

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	30	40	50	60	70
905531	GCTGGGGTGCACGCCTACCNCAGCGGNTCCCCCTTCCTCTTCTGGGAACA				
	::: :: : ***** ***** *****				
hpatched	CTGGGGCTGTCCAGTTACCCCAACGGCTACCCCTTCCTCTTCTGGGAGCA				
	3010	3020	3030	3040	3050

	80	90	100	110	120
905531	GTATCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGCTGTCATCCTGCTGG				
	*** * ***** ** * ** * * ***** * * * * *				
hpatched	GTACATCGGCCTCCGCCACTGGCTGCTGCTGTTTCATCAGCGTGGTGTGG				
	3060	3070	3080	3090	3100

	130	140	150	160	170
905531	TGTGCACTTTCCTCGTCTGTGCTCTGCTGCTCCTNAACCCCTGGACGGCT				
	***** ***** ** * * * * * *****				
hpatched	CCTGCACATTTCCTCGTGTGCGCTGTCTTCCTTCTGAACCCCTGGACGGCC				
	3110	3120	3130	3140	3150

	180	190	200	210	220
905531	GGCCTNATAGTGCTGGTCCTGGCGATGATGACAGTGGAACCTCTTGGTAT				
	** ***** ***** ***** * * * * *				
hpatched	GGGATCATTGTGATGGTCCTGGCGCTGATGACGGTCGAGCTGTTCCGGCAT				
	3160	3170	3180	3190	3200

	230	240	250
905531	CATGGGTTTNCCTGGGCATCAAGCTGAGT		
	***** ** * * * *****		
hpatched	GATGGGCCTCATCGGAATCAAGCTCAGT		
	3210	3220	3230

	80	90	100	110	120
905531	TCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGCTGTCATCCTGCTGGTGT				
	::: ::: * * * * * ***** ***** * * * *****				
hpatched	GCTGCTGCTGTTTCATCAGCGTGGTGTGGCC---TGCACATTTCCTCGTGT				
	3090	3100	3110	3120	

	130	140	150
905531	GCACTTTCCTCGTCTGTGCTCTGCTGCT		
	** * * * * * : :		
hpatched	GCGCTGTCTTCCTTCTGAACCCCTGGAC		
	3130	3140	3150

FIG. 2A

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```

1326258      30      40      50      60      70
GCTGGGGTGCACGCCTACCCCAGCGGCTCCCCCTTCCTCTTCTGGGAACA
      ::: :: : *****
hpatched    CTGGGGCTGTCCAGTTACCCCAACGGCTACCCCTTCCTCTTCTGGGAGCA
      3010      3020      3030      3040      3050

1326258      80      90      100      110      120
GTATCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGG
      *** * ***** * * * * * * * * * * * * * * *
hpatched    GTACATCGGCCTCCGCCACTGGCTGCTGCTGTTTCATCAGCGTGGTGTGG
      3060      3070      3080      3090      3100

1326258      130      140      150
TGTGCACTTTCCTCCTCCTGCTGCTCT
      *****
hpatched    CCTGCACATTCTCGTGTGCGCTGT
      3110      3120      3130

```

```

1326258      90      100      110      120      130
TCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGGTGT
      ::: :: * * * * * * * * * * * * * * *
hpatched    GCTGCTGCTGTTTCATCAGCGTGGTGTGGCC---TGCACATTCTCGTGT
      3090      3100      3110      3120

1326258      140      150
GCACTTTCCTCCTCCTGCTGCTCT
      ** ** ** ***** :
hpatched    GCGCTGTCTTCCTTCTGAACCC
      3130      3140

```

```

1326258      10      20      30      40      50
CCGGGCAGCATGCGCAGAGGCCGGCCAGGCTGGGGTGCACGCCTACCCCA
      ***** * * * * * * * * * * * * * * *
hpatched.RC  CCGGGCGGCATG--GCGAAGCGGACCACGCTGGGGGGTGGCTCAGGGGAG
      710      720      730      740      750

```

FIG. 2B

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PTCH 1 MASAGNAAEPODRGGGGGCGICAGPRPAGGRRRTGGLRRAA[PDRDYL
PTCH2 1MTRSPPLREL.

PTCH 51 HRPSYCDAAFALEQISKGKA[TKRKAPLWLRK][FQRL][F][K][L][G][C][Y][I][K][N][C][G][K]
PTCH2 11 .PPSYTPP..[A]RTAAPQIL[AGSL][KAPLWLRAY][FQGL][FSLGCGI][QRHCGK]

TM1

PTCH 101 F[V][V][G][L][I][F][G][A][F][A][V][G][L][K][A][N][L][E][T][N][V][E][E][L][W][V][E][G][G][R][V][S][R][E][L][N][Y][T][R][Q][K][I][G][E][E]
PTCH2 58 V[F][G][L][I][F][G][A][F][A][V][G][L][K][A][N][L][E][T][N][V][E][E][L][W][V][E][G][G][R][V][S][R][E][L][N][Y][T][R][Q][K][I][G][E][E]

PTCH 151 A[M][F][N][P][Q][L][M][I][Q][T][P][K][E][E][G][A][N][V][L][T][T][E][A][L][L][Q][H][L][D][S][A][L][Q][A][S][R][V][H][V][M][Y][N][R][Q][W][K][L][E]
PTCH2 108 AAYTSQMLIQTAHQEENILTP[EA][L][G][L][H][L][Q][A][L][T][A][S][K][V][Q][V][S][L][Y][G][K][S][W][D][L][N]

PTCH 201 HLCYKSGELIT[ETGYMDQIIIEYLYPCLIITPLDCFWEGAKLQSGTAYLLG
PTCH2 158 KICYKSGVPLIENGMI[EWMI][EKL][FPCVIL][TPLDCFWEGAKLQSGTAYLLG]

PTCH 251 K[P][P][L][R][W][T][N][F][D][P][L][E][F][L][E][E][L][K][K][I][N][Y][Q][V][D][S][W][E][E][M][L][N][K][A][E][V][G][H][G][Y][M][D][R][P][C][L][N][P][A]
PTCH2 208 R[P][D][I][Q][W][T][N][L][D][P][E][Q][L][L][E][E][L][G][P][F][A][S][L][E][G][F][R][E][L][L][D][K][A][Q][V][G][Q][A][Y][V][R][P][C][L][H][P][D]

PTCH 301 [D][P][D][C][P][A][T][A][P][N][K][N][S][T][K][P][L][D][M][A][L][V][L][N][G][G][C][H][G][L][S][R][K][Y][M][H][W][Q][E][E][L][I][V][G][G][T][V][K][N][S]
PTCH2 257 [D][L][H][C][P][P][S][A][P][N][H][H][S][R][Q][A][P][N][V][A][H][E][L][S][G][G][C][H][G][F][S][H][K][F][M][H][W][Q][E][E][L][L][G][G][M][A][R][D][P]

FIG.--3A

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PTCH 351 T G K L V S A H A L Q T M F Q L M T P K Q M Y E H F K G Y E Y V S H . I I N W N E D K A A A I L E A W
PTCH2 307 Q G E L L R A E A L Q S T F L L M S P R Q L Y E H F R G . D Y Q T H D I I G W S E E Q A S T V L Q A W

PTCH 400 Q R T Y V E V V H Q S V A Q N S T Q K V L S F T T T T L D D I L K S F S D V S V R V A S G Y L L M
PTCH2 356 Q R R F V Q L A Q E A L P E N A S Q Q I H A F S S T T L D D I L H A F S E V S A A R V V G G Y L L M

PTCH 450 L A Y A C L T M L R W D C S K S Q G A V G L A G K L L V A L S V A A G L G L C S L I G I S F N A A T
PTCH2 406 L A Y A C V T M L R W D C A Q S Q G S V G L A G Y L L V A L A V A S G L G L C A I L L G I T F N A A T

PTCH 500 T Q V L P F L A L G V C V D D V F L L A H A F S E T G Q N K R I P F E D R T G E C L K R T G A S V A
PTCH2 456 T Q V L P F L A L G I C V D D V F L L A H A F T E A L P G . . T P L Q E R M G E C L Q R T G T S V V

PTCH 550 L T S I S N V T A F F M A A L I P I P A L R A F S L Q A A V V V V F N F A M V L L I F P A I L S M S
PTCH2 504 L T S I N N M A A F L M A A L V P I P A L R A F S L Q A A I V V G C T F E V A V M L V F P A I L S L D

PTCH 600 L Y R R E D R R L D I F C C F T S P C V S R V I Q V E P Q A Y T D T H D N T R Y S P P P P Y S S H S
PTCH2 554 L R R R H C Q R L D V L C C F S S P C S A Q V I Q I L P Q E L G D G T V P V G

PTCH 650 F A H E T Q I T M Q S T V Q L R T E Y D P H T H V Y Y T T A E P R S E I S V Q P V T V T Q D T L S C
PTCH2 593 I A H L T A T V Q A F T H C E A S S Q H V V T I L P P Q A H L V P P P S D P L G S

FIG.-3B

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PTCH 700 QSPESTSSTRDLLSQQFSDSSLH--CLEPPCTKMTLSSFAEKHYAPFLLKP
 PTCH2 634 ELFSPGGSTRDLLGQEEETRQKAACKSLPCARWNLAHFARYQFAPLQLLQS

TM7

PTCH 748 KAKVVFPLGLGLGVSLSYGTTIRVRDGLDLTDIVPRETRETREYDFIAAQFKY
 PTCH2 684 HAKAVVFLVLFCAALLGLSLYGATLVQQDGLALTDVVPRGTKEHAFLSAQLRY

PTCH 798 FSFYNNMYIVTQKA-DYPNIQHLLYDLHRSFSNVKYYVMLEENKQLPKMWLH
 PTCH2 734 FSLYEVALVTQGGFDYAHSCQRALFDLHQRFSSLKAVLPPPATQAPRTWLH

PTCH 847 YFRDWLQGLQDAFDSWETGKIMPNNYKNGSDDGVLAYKLLVQTGSRDKP
 PTCH2 784 YYRNNWLQGIQAADFQDWASGRJTRHSYRNGSEEDGALAYKLLIQTGDAQEP

PTCH 897 IDISQLTKQRLVDAAGIINPSAFYIYLTAWVSNDPVAYAAASQANIRPHRP
 PTCH2 834 LDFSQLTTRKLVDRGLJJPPELFYMGTLTVWVSSDPLGLAASQANFYPPPP

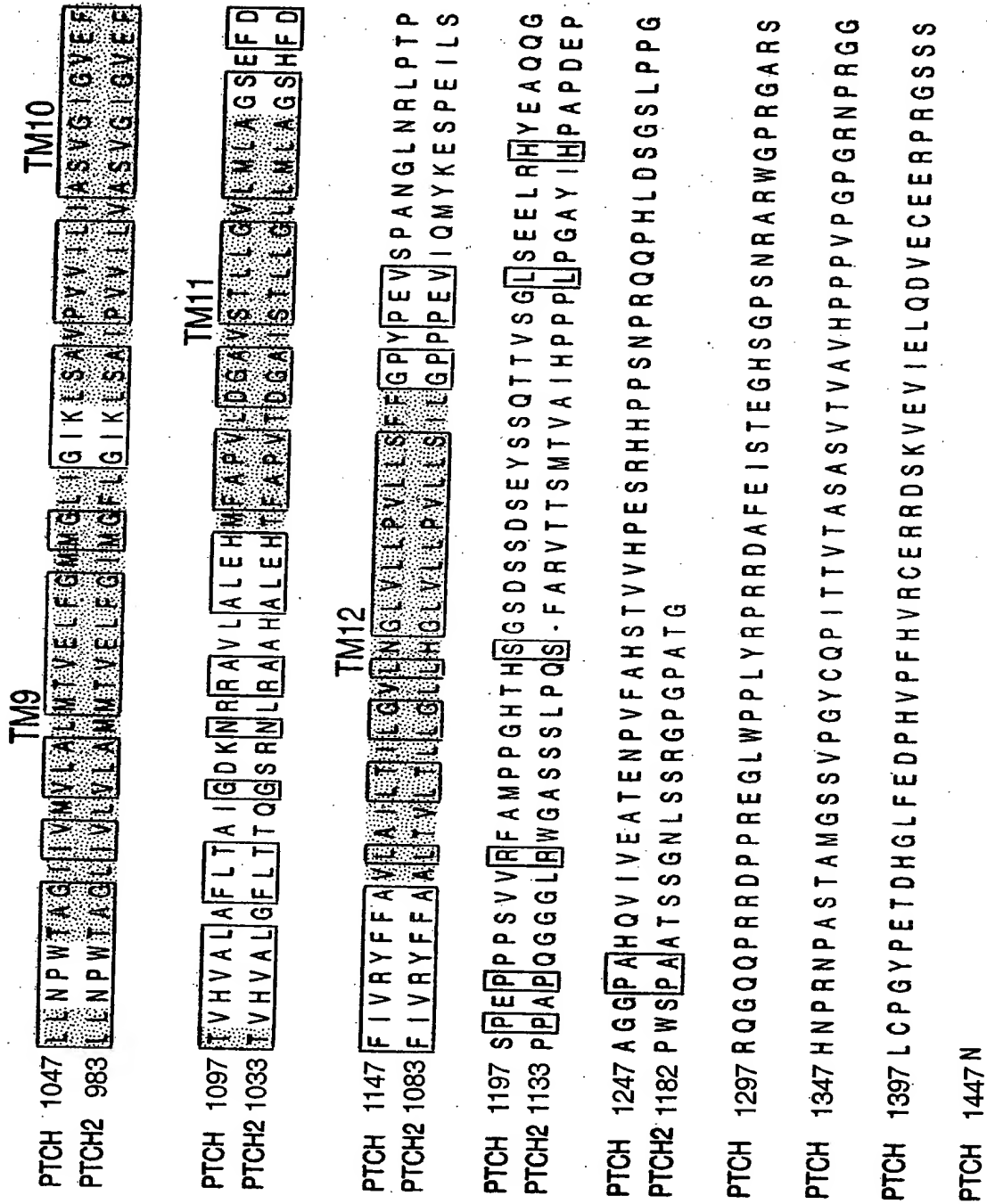
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 PTCH2 884 EWLHDKYD-TTGENLRIPPAQPLEFAQFPFLLRGLQKTDADFVEAIEGAR

TM8

PTCH 997 ICSNYTSLSGLSSYPNGYPPFLFWEQYIIGLRHWLLEFISVVEACTFLVCAYF
 PTCH2 933 ACAEAGQAGVHAYPSGSPFLFWEQYIIGLRRCFLLAVCLLVGTFVLVCALE

FIG.-3C

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**FIG.--3D**

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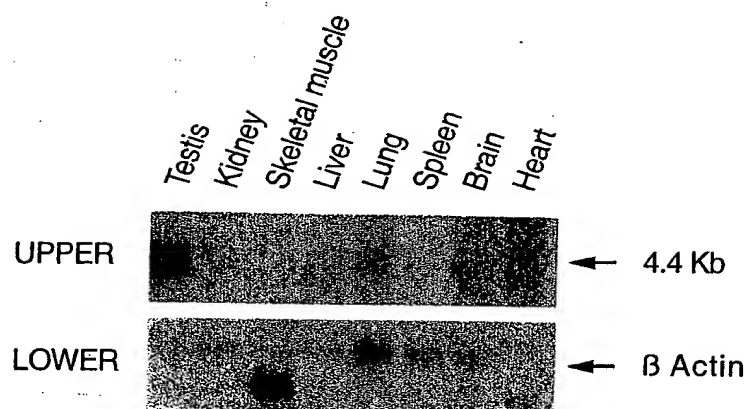


FIG._4

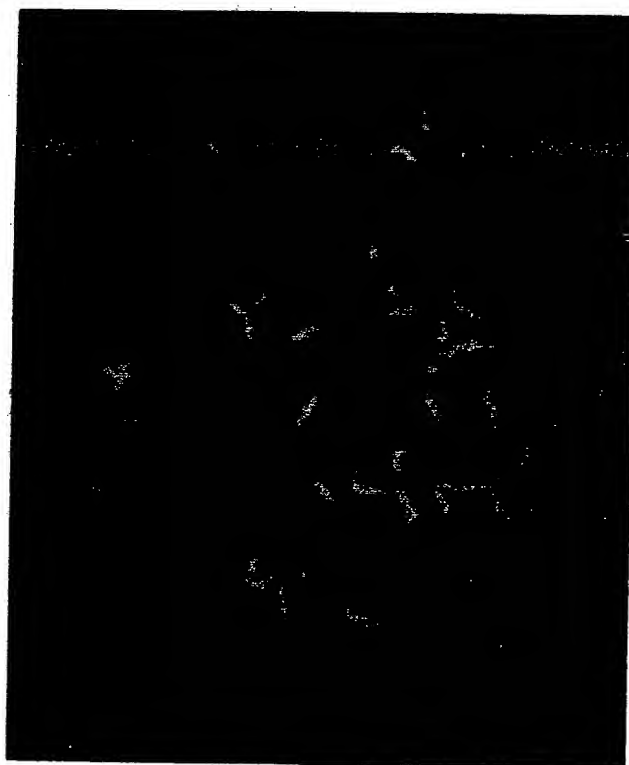


FIG._5

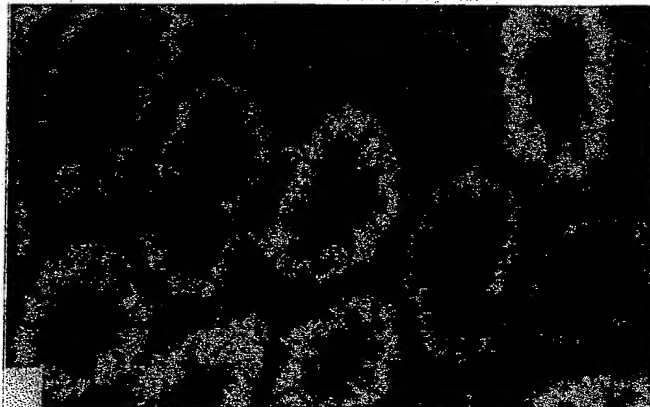


FIG._6C



FIG._6B

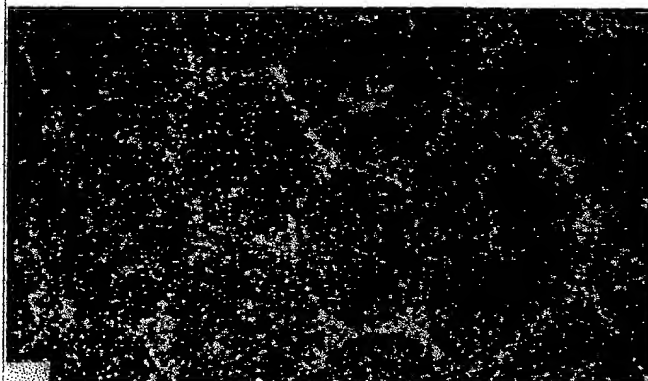


FIG._6A

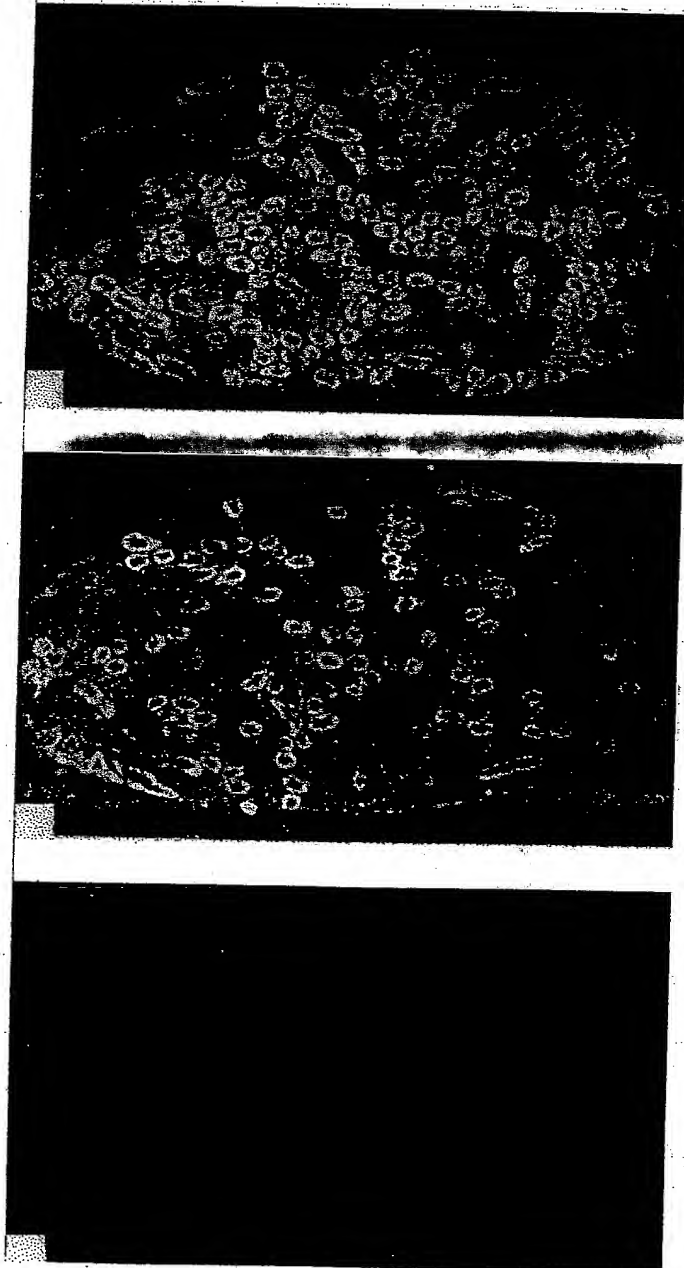
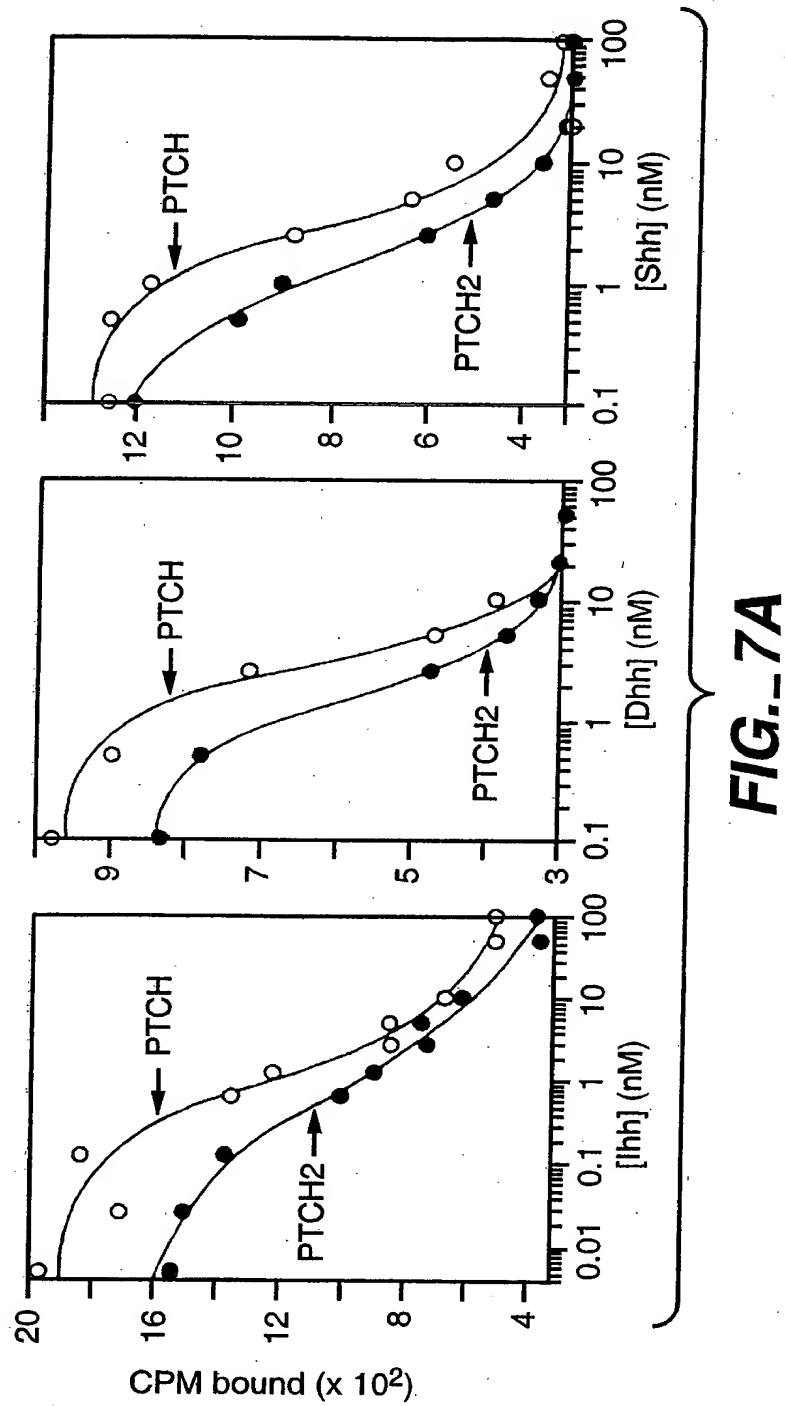


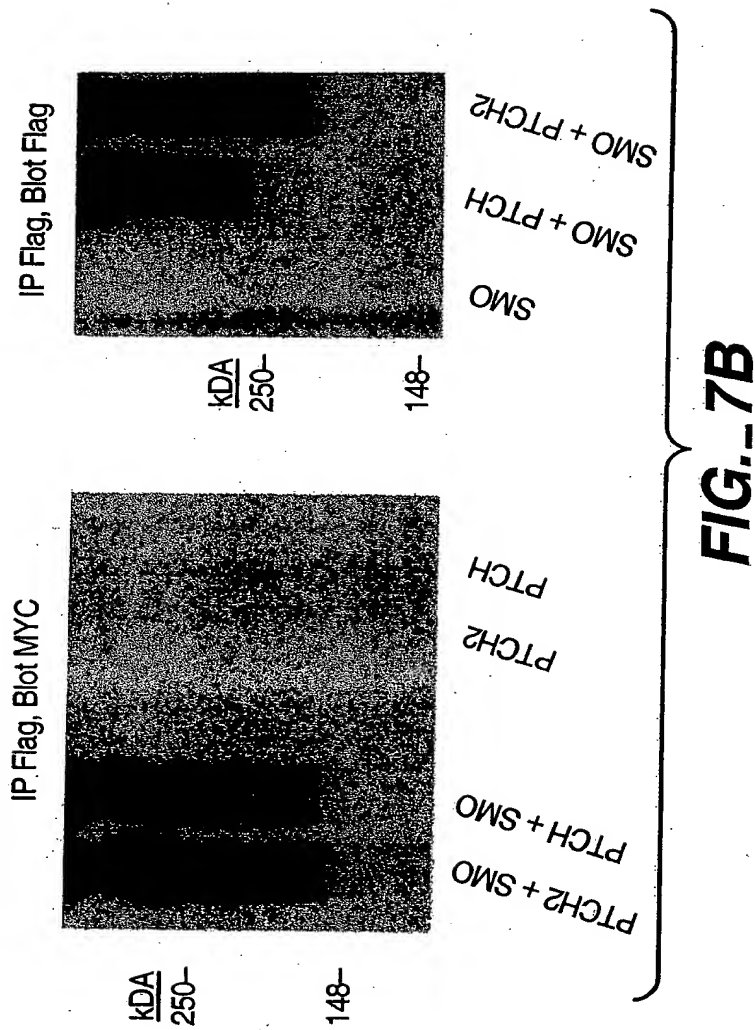
FIG._6F

FIG._6E

FIG._6D

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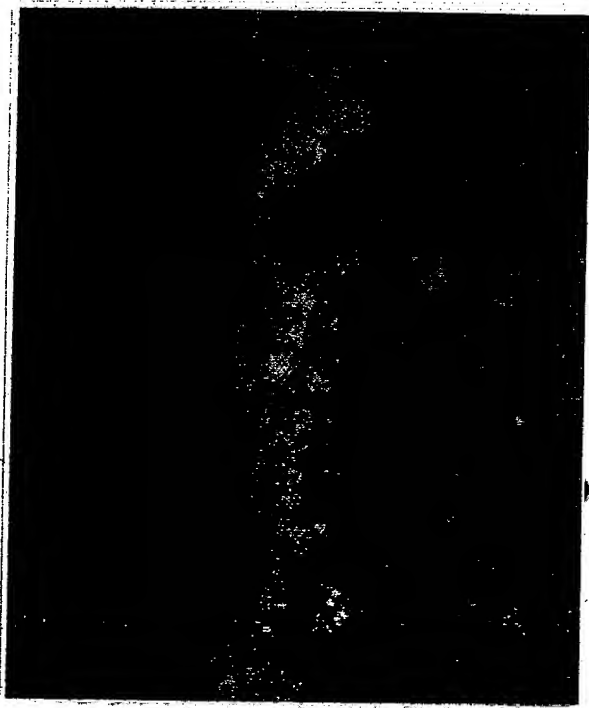
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	10	20	30	40	50
hPitch-2	MTRSPPLRELPPSYTPPARTAAPQILAGSLKAPLWLRAYFQGLLFSLGCG				
mPatched2	MVRPLSLGELPPSYTPPARSSAPHILAGSLQAPLWLRAYFQGLLFSLGCR				
	10	20	30	40	50
	60	70	80	90	100
hPitch-2	IQRHCGKVLFLGLLAFGALALGLRMAIIETNLEQLWVEVGSRVSQELHYT				
mPatched2	IQKHCGKVLFLGLVAFGALALGLRVAVIETDLEQLWVEVGSRVSQELHYT				
	60	70	80	90	100
	110	120	130	140	150
hPitch-2	KEKLGEAAAYSQM LIQTARQEGENILTPEALGLHLQAALTASKVQVSLY				
mPatched2	KEKLGEAAAYSQM LIQTAHQEGGNVLTPEALDLHLQAALTASKVQVSLY				
	110	120	130	140	150
	160	170	180	190	200
hPitch-2	GKSWDLNKICYKSGVPLIENGMI EWMI EKLFPCVILTPLDCFWEGAKLQG				
mPatched2	GKSWDLNKICYKSGVPLIENGMI ERMIEKLFPCVILTPLDCFWEGAKLQG				
	160	170	180	190	200
	210	220	230	240	250
hPitch-2	GSAYLPGRPD IQWTNLDP EQ LLEELGP FASLEG FRELLDKAQVGQAYVGR				
mPatched2	GSAYLPGRPD IQWTNLDP QQLLEELGP FASLEG FRELLDKAQVGQAYVGR				
	210	220	230	240	250
	260	270	280	290	300
hPitch-2	PCLHPDDLHC PPSAPNHHSRQ APNV AHEL SGGCHGF SHKF MHWQEELL LG				
mPatched2	PCLDPDDPHC PPSAPNRHSRQ APNV AQEL SGGCHGF SHKF MHWQEELL LG				
	260	270	280	290	300
	310	320	330	340	350
hPitch-2	GMARD PQGELLRAEALQSTFLLMS PRQLYEHFRGDYQTHDIGWSEEQAST				
mPatched2	GTARDLQGQLLRAEALQSTFLLMS PRQLYEHFRGDYQTHDIGWSEEQASM				
	310	320	330	340	350

FIG. 8A



PTCH2



PTCH

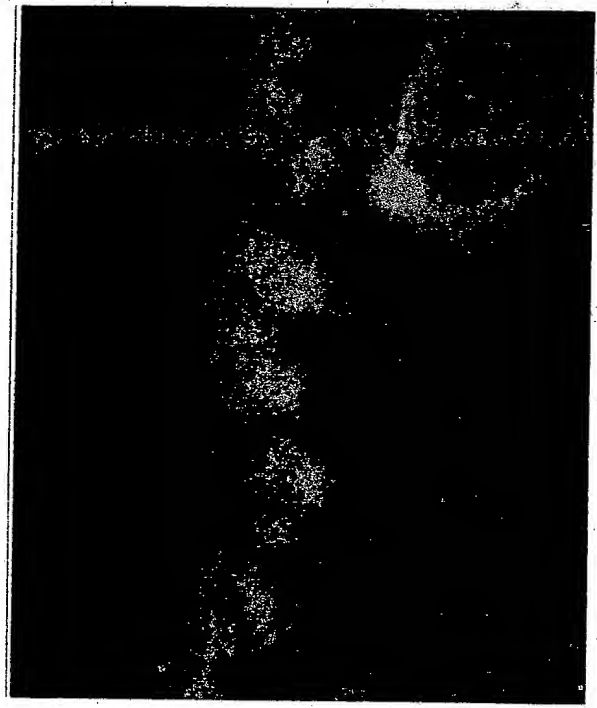


FIG. 9

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GGGTGCGCAG GCCCTCTTCG ACCCCCTCCT CCGACGTATG TGGAGAGTCT ACGACTATGT CTGGCGTGCG GTCTCCCTC TCTGTAGGA GTGTGGGCTT

101 GCACTTGGCC TCCACCTCCA GGCAGCCCTC ACTGCCAGTA AAGTCCAAGT ATCACTCTAT GGGAGTCTT GGAATTTGAA CAAATCTGC TACAAGTCAG
CGTGAACCGG AGGTGGAGGT CCGTCGGGAG TGACGGTCTAT TTCAGGTTC A TAGTGAGATA CCCTTCAGGA CCCTAAACTT GTTTTAGACG ATGTTCAGTC

201 GAGTTCCTT TATTGAAAAT GGAATGATTG AGCGGATGAT TGAGAAGCTG TTTCCGTGCG TGATCTCTAC CCCCTCGAC TGCTTCTGGG AGGGAGCCAA
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301 ACTCCAAGGG GGCTCCGCT ACCTGCCGCT CCCAATGTGG CTCACGAGCT GAGTGGGGG TGCCATGGCT TCTCCACAA ATTCTGCAC TGGCAGGAGG
TGAGGTTCCC CCGAGGCGGA TGGACGGCGA GGGTTACACC GAGTGTCTGA CTCACCCCG ACGGTACCGA AGAGGTGTT TAAGTAGTG ACCGTCCTCC

401 AATTGCTGCT GGGAGGCATG GCCAGAGACC CCCAAGGAGA GCTGCTGAGG GCAGAGGCCC TGCAGAGCAC CTTCTTGCTG ATGAGTCCC GCCAGCTGTA
TTAAGGACGA CCTCCGTAC CGGTCTCTGG GGGTTCTCTT CGACGACTCC CGTCTCCGG ACGTCTCGTG GAAGAACGAC TACTCAGGGG CGGTGACAT

501 CGAGCATTC CGGGTGACT ATCAGACACA TGACATTGGC TGGAGTGAGG AGCAGGCCAG CACAGTGCTA CAAGCCTGGC AGCGGCGCTT TGTGCAGGTC
GCTCGTAAAG GCGCCACTGA TAGTCTGTGT ACTGTAACCG ACCTCACTCC TCGTCCGGTC GTGTACAGAT GTTCGGACCG TCGCCGCGAA ACACGTCCAG

601 GGTATGGACA AGGACAGGG GGTGCCCTGA GGCCATTCCC TCTCTCTGCC CCTCTCTATC CACCTGTTT CTCCAGCTGG CCCAGGAGGC CCTGCTCTGAG
CCATACCTGT TCCTGTCCCC CCACGGGACT CCGGTAAGG AGGAGGACGG GGGAGGATAG GTGGGACAAA GAGGTGACCG GGGTCTCTCCG GGACGGGACTC

FIG. 10A

701 AACGCTTCCC AGCAGATCCA TGCCCTTCTCC TCCACCACCC TGGATGACAT CCTGCATGCG TTCTCTGAAG TCAGTGCTGC CCGTGTGGTG GGAGGCTATC
TTGCGAAGGG TCGTCTAGGT ACGGAAGAGG AGGTGGTGGG ACCTACTGTA GGACGTACGC AAGAGACTTC AGTCACGACG GGCACACCAC CCTCCGATAG

801 TGCTCATGTT GGGTCTTGCA CCTGGCACTT TGCCCCCACC CCACCTCCAA CCAGTGCCCA CCCTGGGAG CCCCTGAGAC TGCCTTTTCC CCCCACAGCT
ACGAGTACCA CCCAGAACGT GGACCGTGGA ACGGGGGTGG GGTGGAGGTT GGTACAGGGT GGGACCCCTC GGGGACTCTG ACGGGAAGG GGGGTGTGGA

901 GGCCTATGCC TGTGTGACCA TGCTGCGGTG GGA CTGGCC CAGTCCCAGG GTTCCGTGGG CCTTGCCGGG GTACTGCTGG TGGCCCTGGC GGTGGCCCTCA
CCGGATACGG ACACACTGGT ACGACGCCAC CTTGACGCGG GTCAGGTCC CAAGGCACCC GGAACGGCCC CATGACGACC ACCGGGACCG CCACCGGAGT

1001 GGCCTTGGGC TCTGTGCCCT GCTCGGCATC ACCTTCAATG CTGCCACTAC CCAGGTACGC CAGGACTGCA GGGCAGACTC AGTGCCAGTC ACCAGGCTTC
CCGGAACCCG AGACACGGGA CGAGCCGTAG TGAAGTTAC GACGGTGATG GTTCCATGCG GTCTTGACGT CCCGTCTGAG TCACGGTCTAG TGGTCCGAAG

1101 ACGGTCCTC AGTGCCCGC TCCTCTGCC CTCCAGGTGC TGCCCTTCTT GACTCTGGA ATCGCGGTGG ATGACGTATT CCTGTGGCG CATGCCCTCA
TGCCCAAGG TCGACGGGCG AGGACACGGG GAGGTCCACG ACGGGAAGAA CTGAGACCCT TAGCCGACCC TACTGCATAA GGACGACCG GTACCGAAGT

1201 CAGAGGCTCT GCCTGGCACC CCTCTCCAGG TGGGGCCTTG TCCCCCAGG CTCATCTGAG GCAGCTCAGC TTA CTGGTTA AGAGCCTCTT GGTTCAGTG
GTCTCCGAGA CGGACCGTGG GGAGAGGTCC ACCCCGGGAC AGGGGGTCCC GAGTAGACTC CGTCGAGTCG AATGACCAAT TCTCGGAGAA CCAAGTTTAC

1301 ACCTTGGGCT GCTAATGAAC CTCGGTGCCT CTTGTCCCA TGTGTAAACA GGGAAATAA TAGTGCTGTG TCCTAAGGGT TATTGTTGG ATCAGTGAAG
TGGAAACCGA CGATTACTTG GAGCCACGGA GAACAGGGGT ACACATTTGT CCCCTTTATT ATCAGACAC AGGATTCCCA ATAACAACCC TAGTCACTTC

1401 TAACTCAAGT TGAATGCTTA GAACAGCCCC TCATACGTAC ATGGTACCA ATAAATGCTA GCCACTGTGT TATGACTGCC CCACCTCTGC ACCCCAAGTT
ATTGAGTTCA ACTTACGAAT CTTGTGCGGT AGTATGCATG TACCATGGGT TATTACCAT CCGTGACACA ATACTGACGG GGTGGAGACG TGGGGTTCAA

FIG.-10B

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1501 CCTGAGCCTC CCCTTCACTC CACITTTGACA CGGCCCTCTC CTTGTGACCT GAGGCAGGT CCCCACTCTG TCCTGGCAGG AGCGCATGGG CGAGTGTCTG
GGACTCGGAG GGGAACTGT GTGAACTGT GCGGGGAGG GAACACTGGA CTCCTGTCGA GGGGTGAGAC AGGACCGTCC TCGGTATACC GCTCACAGAC

1601 CAGCGCACGG GCACCACTGT TGTACTCACA TCCATCAACA ACATGGCCGC CTTCTCTCATG GCTGCCCTCG TTCCCATCCC TCGGCTGCGA GCCTTCTCCC
GTGCGGTGCC CGTGGTCACA ACATGAGTGT AGGTAGTTGT TGTACGGCG GAAGGAGTAC CGACGGGAGC AAGGGTAGGG ACGGACGCT CGGAAGAGGG

1701 TACAGCCTGG ACCTACGGG GCGCCACTGC CAGGCCCTTG ATGTGCTCTG CTGCTTCTCC AGGTACTGCC TCGGCCCCAG CCCCTTCTC CCGTGACCCA
ATGTGGACC TGGATGCCGC CGCGGTGACG GTCGCGGAAC TACACGAGAC GACGAAGAGG TCCATGACGG ACGCGGGGTC GGGGAAGGAG GGCATGGGT

1801 CGCCAGCCTG TCCCCTCACC AGCATTTCAA GGCACAGACC TGTATCCAC TTCTACCTC TTCCAGTCCC TGCTCTGCTC AGGTGATTCA GATCTGCCCC
GCGGTGGGAC AGGGGAGTGG TCGTAAAGTT CCGTGTCTGG ACAGTAGGTG AGAGATGGAG AAGGTCAGGG ACGAGACGAG TCCACTAAGT CTAGGACGGG

1901 CAGGAGCTGG GGGACGGGAC AGTACCAGTG GGCATTGCCC ACCTCACTGC CACAGTTCAA GCCTTTACCC ACTGTGAAGC CAGCAGCCAG CATGTGTTCA
GTCCTCGACC CCTGCCCCG TCATGGTTCAC CCGTAACGGG TGGAGTGACG GTGTCAAGTT CGGAATGGG TGACACTTCG GTCGTGCTC GTACACCAGT

2001 CCATCTCTGC TCCCAAGCC CACCTGGTGC CCCCACCTTC TGACCCACTG GGTCTGAGC TCTTCAGCCC TGGAGGTCC ACACGGGACC TTCTAGGCCA
GGTAGGACGG AGGGTTTGG GTGGACCACG GGGGTGGAAG ACTGGGTGAC CCGAGACTCG AGAGTCTGG ACCTCCGAGG TGTGCCCTGG AAGATCCGGT

2101 GGAGGAGGAG ACAAGGCAGA AGGCAGCCTG CAAGTCCCCTG CCTGTGCCC GGTGGAATCT TGCCCATTTT GCGCGCTATC AGTTTGCCCC GTTGTCTCTC
CCTCCTCCTC TGTTCGGTCT TCCGTGCGAC GTTCAGGGAC GGCACACGGG CGACCTTAGA ACGGGTAAAG CCGGGCGATAG TCAACCGGG CAACGACGAG

2201 CAGTCACATG CCAAGGCCAT CGTGTGTTGG CTCTTCTGGG CTTGAGCCTC TACGGAGCCA CCTTGTGTCA AGACGGCCTG GCCCTGACGG
GTCAGTGTAC GGTTCGGTA GCACGACCAC GAGAAACCAC GAGAGACCC GGAAGACCG ATGCTCGGT GGAACCAAGT TCTGCCGGAC CGGGAAGTGG

FIG. 10C

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2301 ATGTGGTGCC TCGGGGCACC AAGGAGCATG CCTTCCTGAG CGCCACAGTC AGTACTTCT CCTGTACGA GGTGGCCCTG GTGACCCAGG GTGGCTTTGA
TACACCACGG AGCCCGGTGG TTCTCTGTAC GGAAGGACTC GCGGTCGAG TCCATGAAGA GGGACATGCT CCACCGGGAC CACTGGGTCC CACCGAAACT

2401 CTACGCCCCA TCCCAACGGC CCCTCTTTGA TCTGCACCAG CGCTTCAGTT CCTCAAGGC GGTGCTGCCC CCACCGGCCA CCCAGGCACC CCGCACCTGG
GATCGGGTG AGGGTTGGC GGGAGTGGC AGACGTGGTC GCGAAGTCAA GGGAGTTCCG CCACGACGGG GGTGCCGGT GGTCCGTGG GCGCTGGACC

2501 CTGCACTATT ACCGCAACTG GCTACAGGGA ATCCAGGCTG CCTTTGACCA GGAAGTGGT TCTGGGGCA TCACCGGCCA CTCGTACCGC AATGGCTCTG
GACGTGATAA TGGCGTTGAC CGATGTCCCT TAGGTCCGAC GGAAGTGGT CCTGACCCGA AGACCGCGT AGTGGGGGT GAGCATGGC TTACCGAGAC

2601 AGGATGGGC CCTGGCCTAC AAGTGCTCA TCCAGACTGG AGACGCCAG GAGCCTCTGG ATTTACCCA GGTGGGAGA GGGCTGGAGG GGTCCACTAG
TCCTACCCCG GGACCGGATG TTGACGAGT AGGTCTGACC TCTGCGGTC CTCGGAGACC TAAAGTCGT CCAACCTCTT CCGACCTCC CCAGGTGATC

2701 TACAGGGGCT GCAGGCCTCC TGGGCCCAGG CCTTCAGCCC TCTCTGCCTC TGCAGCTGAC CACAAGGAAG CTGGTGGACA GAGAGGACT GATTCACCC
ATGTCCCGA CGTCCGGAGG ACCCGGGTCC GGAAGTCGGG AGAGACGGAG ACCTGACTG GTGTTCTTC GACCACCTGT CTCTCCCTGA CTAAGGTGGG

2801 GAGCTCTTCT ACATGGGGCT GACCGTGTGG GTGAGCAGTG ACCCCCTGGG TCTGGCAGCC TCACAGGCCA ACTTCTACCC CCCACCTCTT GAATGGCTGC
CTCGAGAAGA TGTACCCCGA CTGGCACACC CACTCGTCAC TGGGGGADCC AGACCGTCGG AGTGTCCGT TGAAGATGG GGGTGGAGA CTTACCGAGC

2901 ACGACAAATA CGACACCACG GGGGAGAACC TTCCAGTGA GTCTTGGGG GAGTCGGCA AGAGCCTCAG CCTCGCCAC ACAAGCCCTG AGCCTGAGGC
TGCTGTTTAT GCTGTGTGTC CCCCTCTTGG AAGCGTCACT CAGAACCCCT CTCGGAGTC TCTCGGGTG GGAGCGGTG TGTTCGGAC TCGGACTCCG

3001 CCTGCCCCACT CTGCCCGGTG CTCACCGCCC TGTCCCTCTC CCTCTTCTCC CTTCCCTCC CCTCCACAGT CCCGCCAGT CAGCCCTGG AGTTGCCCCA
GGACGGGTGA GACGGGCAC GAGTGGCGG ACAGGGAGAG GGAGAGAGG GAAGGGAGG GGAGTGTCA GGGCGGTCA GTCGGGAACC TCAACGGGT

FIG. 10D

3101 GTTCCCTTC CTGCTGCTG GCCTCCAGAA GACTGCAGAC TTITGGAGG CCATCGAGGG GGCCCGGGCA GCATGCGCAG AGGCCGGCCA GGCTGGGGTG
CAAGGGGAAG GACGACGCAC CGGAGTCTT CTGACCTCTG AATACCTCC GGTAGCTCC CCGGCCCGT CCGGCCCGT TCCGGCCCGT CCGACCCAC

3201 CACGCCTACC CCAGCGGCTC CCCCTTCTC TTCTGGGAAC AGTATCTGG CCTGGGGGC TGTTCCTGC TGGCCGTCTG CATCTGCTG GTGTGCACTT
GTGCGGATGG GGTGCGCGAG GGGGAGGAG AAGACCTTG TCATAGACC GGACGCCGG ACAGGAGC ACCGGCAGC GTAGGACGAC CACACGTGAA

3301 TCCTCGTCTG TGCTCTGCTG CTCCTCAACC CCTGGACGGC TGGCCTCATA GTGATGCTT GCAGGAGTG GGACAGAGC ACCCCACCT TCCCTGCCCA
AGGAGCAGAC ACGAGACGAC GAGGAGTTG GGACCTGCC AGCGAGTAT CACTCAGAA CTCCTCACC CCTGTCTCTG TGGGTGGA AGGGACGGT

3401 GCCTGTCTC CCTCCTGCCA GGAGCCCTCT GTGAGCCCTG TCTCCCTCAG GTGCTGCTC TGGCGATGAT GACAGTGGAA CTCCTTGGTA TCATGGGTTT
CGGACAGTAG GGAGGACGGT CCTCGGGAGA CACTCGGGAC AGAGGGAGT CACGACGAG CACGACGAG ACCGCTACTA CTGTACCTT GAGAAACCAT AGTACCCAAA

3501 CCTGGGCATC AAGCTGAGT CCATCCCGT GGTGATCCTT GTGGCCTCTG TAGGCATTG CATTGAGTTC ACAGTCCAG TGGCTCTGGT GAGCAGGGC
GGACCCGCTG TTGACTCAG GGTAGGGCA CCACTAGGAA CACCGGAGC ATCCGTAAC GCAACTCAAG TGTGAGTGC ACCGAGACCA CTCGTGCCCC

3601 ACCCCGGGGA GGGACCAATC AGCTGATTCA GTATTCAACA CATATTGTC AAGCCCTAC TATGTGCTAG GTACTATTTA AGAATTGGG CTGGGTGGAC
TGGGGCCCT CCCTGGTTAG TCGACTAAGT CATPAGTTGT GTATAACAAG TTCGGGGATG ATACAGATC CATGATAAAT TCTTAAACCC GACCCACCTG

3701 GTGGTGGCTC ATTCCTGTAA TCCAGCACT TTGGGAGGCC GAGCGGGTG GATCACCTGA GGTGCGGAGT TCGAAACAG CCTGGCCAAC ATGTGAAAC
CACCACCGAG TAAGACATT AGGTGCTGA AACCTCCGG CTCGGCCAC CTAGTGGACT CCAGCCCTCA AGCTTTGGT GACCCGGTGG TACCACTTG

3801 CCTGTCTTTA CTAATAATAC AAAAAATTAG CCAGCGGTGG TGGCACATGC CAGTAGTCCC AGCTACTTTG GAGGCTGAGG CAGAAATGCT TGAACCTGGG
GGACAGAAAT GATTTTATG TTTTAAATC GGTCCGCACC ACCGTGTACG GTCATCAGG TCGATGAAAC CTCGACTCC GTCTTAAAGA ACTTGGACCC

3901 AGGCGAAGT TGAGTGAGC TGAGATCGTG CCATTGCACT CCAGCTGGG CAACAAGAGT GCAACTCTCC GTCTCAAAA AAAAAAAA AAGGGCGGCC
TCCGCTTCCA AGTCACTCG ACTTAGCAC GGTAACTGA GGTGAGGCC GTTGTCTCA CGTTGAGAGG CAGAGTTTTT TTTTTTTTTT TTCCCGCCGG

4001 GCGA
CGCT

FIG.-10E

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1 TTCCGGCATG ACTCGATCGC CGCCCTCAG AGAGCTGCCC CCGAGTTACA CACCCCCAGC TCGAACCGCA GCACCCACAGA TCCTAGCTGG GAGCCTGAAG
AAGGCCGTAC TGAGCTAGCG GCGGGGAGTC TCTCGACGGG GGCTCAATGT GTGGGGGTCT AGCTTGGCGT CGTGGGTCT AGGATCGACC CTCGGACTTC

101 GCTCCACTCT GGCTTCGTGC TTAATTCCAG GGCCTGCTCT TCTCTCTGG ATGCGGATC CAGAGACATT GTGGCAAGT GCTCTTTCTG GGACTGTTGG
CGAGGTGAGA CCGAAGCAGC AATGAAGGTC CCGGACGAGA AGAGAGACCC TAGCCCTAG GTCTCTGTAA CACCGTTTCA CGAGAAAGAC CCTGACAACC

201 CCTTTGGGGC CCTGGCATTG GGTCTCCGCA TGGCCATTAT TGAGACAAAC TTGGAACAGC TCTGGGTAGA AGTGGGCAGC CGGGTGAGCC AGGAGCTGCA
GGAAACCCCG GGACCGTAAT CCAGAGGCGT ACCGGTAATA ACTCTGTTG AACCTTGTCG AGACCCATCT TCACCCGTCG GCCCACTGG TCCTCGACGT

301 TTACACCAAG GAGAAGCTGG GGGAGGAGGC TGCATACACC TCTCAGATGC TGATACAGAC CGCAGGCCAG GAGGGAGAGA ACATCCTCAC ACCCGAAGCA
AATGTGGTTC CTCTTCGACC CCTCTCTCCG ACGTATGTGG AGAGTCTACG ACTATGTCG GCGTGCGGTC CTCCCTCTCT TGTAGGAGTG TGGGCTTCGT

401 CTTGGCCTCC ACCTCCAGC AGCCCTCACT GCCAGTAAAG TCCAAGTATC ACTCTATGGG AAGTCTGGG ATTGAACAA AATCTGCTAC AAGTCAGGAG
GAACCGGAGG TGGAGGTCCG TCGGGAGTGA CCGTCATTTC AGGTTCAATAG TGAGATACCC TTCAGGACCC TAAACTTGTT TTAGACGATG TTCAGTCCTC

501 TTCCCTTAT TGAANAATGA ATGATTGAGT GGATGATTGA GAAGCTGTTT CCGTGGGTGA TCCTCACCCC CCTCGACTGC TTCTGGGAGG GAGCCAAACT
AAGGGGAATA ACTTTTACCT TACTAACTCA CCTACTAACT CTTGACAAA GGCACGCACT AGGAGTGGG GGAGCTGACG AAGACCTCC CTCGGTTTGA

FIG. 11A

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601 CCAAGGGGC TCCGCCTACC TGCCCGGCGG CCGGATATC CAGTGGACCA ACTGGATCC AGAGCAGCTG CTGGAGGAGC TGGGTCCCTT TGCCTCCCTT
GGTTCCCGG AGGCGGATGG ACGGCGCGG GGCCTATAG GTCACCTGGT TGGACCTAGG TCTCGTCGAC GACCTCCTCG ACCCAGGGAA ACGAGGGAA

701 GAGGGCTTC GGGAGCTGCT AGACAAGGCA CAGGTGGGCC AGGCCTACGT GGGCGGCCC TGTCTGCACC CTGATGACCT CCAC TGCCCCA CCTAGTGCCC
CTCCGAAGG CCCTCGACGA TCTGTTCCGT GTCCACCCGG TCCGGATGCA CCCCCCGG ACAGACGTGG GACTACTGGA GGTACGGGT GGATCAGGGE

801 CCAACCATCA CAGCAGGCAG GCTCCCAATG TGGCTCAGCA GCTGAGTGG GGTGCCATG GCTTCTCCA CAAATTCATG CACTGGCAGG AGGAATTGCT
GGTTGGTAGT GTCGTCCGTC CGAGGGTTAC ACCGAGTGCT CGACTCACCC CCGACGCTAC CGAAGAGGGT GTTAAAGTAC GTGACCGTCC TCCTTAACGA

901 GCTGGGAGGC ATGGCCAGAG ACCCCCAAGG AGAGCTGCTG AGGCAGAGG CCCTGCAGAG CACCTTCTTG CTGATGAGTC CCCGCCAGCT GTACGAGCAT
CGACCCTCCG TACCGGTCTC TGGGGTTCC TCTCGAGAC TCCCGTCTCC GGGACGTCTC GTGAAGAAC GACTACTCAG GGGCGGTCCA CATGCTCGTA

1001 TTCCGGGGTG ACTATCAGAC ACATGACATT GGTGGAGTG AGGAGCAGGC CAGCACAGTG CTACAAGCCT GGCAGCGGCG CTTTGTGCAG CTGGCCCCAGG
AAGGCCCCAC TGATAGTCTG TGTAAGTCTG CCGACCTCAC TCTCTGCTCC GTCGTGTCAC GATGTTCCGA CCGTCGCCG GAAACACGTC GACCGGGTCC

1101 AGGCCCTGCC TGAGAACGCT TCCCAGCAGA TCCATGCTCTT CTCCTCCACC ACCCTGGATA ACATCCTGCA TCGTCTCTCT GAATCAGTG CTGCCCCGTGT
TCCGGGACGG ACTCTTGCGA AGGTCTGCT AGGTACGGAA GAGGAGGTGG TGGACCTAT TGTAGGACGT ACACAAGAGA CTTCACTCAC GACGGGCACA

1201 GGTGGGAGGC TATCTGCTCA TGCTGGCCTA TGCTGTGTG ACCATGCTGC GGTGGGACTG CGCCCAGTCC CAGGGTTCCG TGGGCTTGC CGGGGTACTG
CCACCCTCCG ATAGACGAGT ACGACCGGAT ACGGACACAC TGGTACGAG CCACCTGAC GCGGGTCAGG GTCCCAAGGC ACCCGGAACG GCCCCATGAC

1301 CTGGTGGCCC TGGGGTGGC CTCAGGCCCTT GGGCTCTGTG CCTGCTCGG CATCACCTTC AATGCTGCCA CTACCAGGT GCTGCCCTTC TTGGCTCTGG
GACCACCGG ACCGCCACCG GAGTCCGGAA CCGGAGACAC GGGACGAGCC GTAGTGAAG TTAGACGCT GATGGTCCA CGACGGGAAG AACCGAGACC

FIG. 11B

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1401 GAATCGGCGT GGATGACGTA TTCCTGCTGG CGCATGCCTT CACAGAGGCT CTGCCTGGCA CCCCTCTCCA GGAGCGCATG GCGAGTGTTC TGCAGCGCAC
CTTAGCCGCA CCTACTGCAT AAGGACGACC GCGTACGGAA GTGTCTCCGA GACGGACCGT GGGGAGAGGT CCTCGCGTAC CCGTCCACAG ACGTCGCGTG

1501 GGGCACCAGT GTCGTACTCA CATCCATCAA CAACATGGCC GCCTTCCTCA TGGCTGCCCT CGTTCCCATC CCTGCGCTGC GAGCCTTCTC CTTACAGCCA
CCCCGTGGTCA CAGCATGAGT GTAGGTAGTT GTTGTACCGG CGGAAGGAGT ACCGACGGGA GCAAGGGTAG GGACGCGACG CTCGGAAGAG GAATGTGCGT

1601 TCCTCAGCCT GGACCTACGG CGGCGCCACT GCCAGCGCCT TGATGTGCTC TGCTGCTTCT CCAGTCCCTG CTCTGCTCAG GTGATTCAGA TCCTGCCCCCA
AGGAGTCGGA CCTGGATGCC GCCGCGGTGA CCGTCGGGGA ACTACACGAG ACGACGAAGA GGTACGGGAC GAGACGAGTC CACTAAGTCT AGGACGGGGT

1701 GGAGCTGGGG GACGGGACAG TACCAGTGGG CATTGGCCAC CTCACTGCCA CAGTTCAAGC CTTTACCCAC TGTGAAGCCA GCAGCCAGCA TGTGTCACC
CCTCGACCCC CTGCCCTGTC ATGGTCACCC GTAACGGGTG GAGTGACGGT GTCAAGTTGG GAATGGGTG ACACTTCGGT CGTCGGTCGT ACACCAGTGG

1801 ATCTGCTC CCCAAGCCCA CCTGGTGCCC CCACCTTCTG ACCCACTGGG CTCTGAGCTC TTCAGCCCTG GAGGGTCCAC ACGGGACCTT CTAGGCCAGG
TAGGACGGAG GGGTTCGGT GGACCACGGG GGTGGAAGAC TGGGTGACCC GAGACTCGAG AAGTCGGGAC CTCCCAGGTG TGCCCTGGAA GATCCGGTCC

1901 AGGAGGAGAC AAGGCAGAAG GCAGCCTGCA AGTCCCTGCC CTGTGCCCGC TGAATCTTG CCCATTTCG CCGGAATTC CTGCAGCCCG GGGGATCCAC
TCCTCCTCTG TTCCGTCTTC CGTCGGACGT TCAGGGACGG GACACGGGG ACCTTAGAAC GGGTAAAGCG GGGCCCTTAAG GACGTGCGGC CCCCTAGGTG

2001 TAGTTCTAGA GCGGCCGCCA CCGCGGTGGA GCTCCAGCTT TTGTTCCCTT TAGTAGGGT TAATTGGCG CTTGSGTATC TT
ATCAAGATCT CGCCGGCGGT GCGGCCACCT CGAGGTCGAA AACAGGGAA ATCACTCCCA ATTAACGCGC GAACCCATAG AA

FIG.-11C

1 GTTATTTTCAG GCCATGGTGT TGCGCCGAAT TAATTCCCGA TCCAGACATG ATAAGATACA TTGATGAGTT TGGACAAACC ACAACTAGAA TGCAGTGA
CAATAAAGTC CGGTACCACA ACGCGGCTTA ATTAAGGCTT AGTCTGTAC TATTCTATGT AACTACTCAA ACCTGTTGG TGTGATCTT ACGTCACCTT

~~sequence~~

101 AAAATGCTTT ATTTGTGAAA TTTGTGATGC TATTGCTTTA TTTGTAACCA TTATAAGCTG CAATAAACAA GTTGGGCCAT GGCGGCCAAG CTTCTGCAGG
TTTACGAAA TAAACACTTT AAACACTAGC ATAACGAAAT AAACATTGGT AATATTGAC GTTATTGTT CAACCCGGTA CCGCCGGTTC GAAGACGTCC

201 TCGACTCTAG AGGATCCCCG GGGAAATTCG GCATGACTCG ATCGCCGCC CTAAGAGAGC TGCCCGCGAG TTACACACCC CCAGCTCGAA CCGCAGCACC
AGCTGAGATC TCCTAGGGG CCGTTAAGGC CGTACTGAGC TAGCGCGGG GAGTCTCTCG ACGGGGCTC AATGTGTGG GGTGAGCTT GCGTCTGTGG

1 M T R S P P L R E L P P S Y T P P A R T A A P
~~insert starts here~~ (SEQUENCE)

301 CCAGATCCTA GCTGGGAGCC TGAAGGCTCC ACTCTGGCTT CGTCTTACT TCCAGGGCCT GCTCTTCTCT CTGGGATGCG GGATCCAGAG ACATTGTGGC
GGTCTAGGAT CGACCTCTCG ACTTCCGAGG TGAGACCGAA GCACGAATGA AGGTCCCGGA CGAGAAGAGA GACCTACGC CCTAGGTCTC TGTAAACACCG

24 Q I L A G S L K A P L W L R A Y F Q G L L F S L G C G I Q R H C G
401 AAAGTGCTCT TTCTGGGACT GTTGGCCTTT GGGGCCCTGG CATTAGGTCT CCGATGGCC ATTATTGAGA CAAACTTGA ACAGCTCTGG GTAGAAGTGG

TTTCACGAGA AAGACCTGA CAACCGGAAA CCGCGGACC GATATCCAGA GCGTACCGG TAATAACTCT GTTGAACCT TGTGAGACC CATCTTCACC
57 K V L F L G L L A F G A L A L G L R M A I I E T N L E Q L W V E V G

501 GCAGCCGGGT GAGCCAGGAG CTGCATTACA CCAAGGAGAA GCTGGGGAG GAGGTGCGAT ACACCTCTCA GATGCTGATA CAGACCGCAC GCCAGGAGGG
CGTCGGCCCA CTCGGTCTC GACGTAATGT GTTCTCTCTT CGACCCCTCT CACCGACGTA TGTGGAGAGT CTACGACTAT GTCTGGCGTG CCGTCTCTCC

91 S R V S Q E L H Y T K E K L G E E A A Y T S Q M L I Q T A R Q E G
601 AGAGAACATC CTCACACCCG AAGCACCTTG CCTCCACCTC CAGCAGCCCT TCACTGCCAG TAAAGTCCAA GTATCACTCT ATGGGAAGTC CTGGGATTG

TCTCTTGTAG GAGTGTGGC TTCTGTGACC GGAGGTGGAG GTCCGTCCGG AGTGACGCTC ATTTTCAGGT CATAGTGAGA TACCCTTCAG GACCTAAAC
124 E N I L T P E A L G L H L Q A A L T A S K V Q V S L Y G K S W D L

701 AACAAAATCT GCTACAAAGTC AGGAGTTCCC CTTATTGAAA ATGGAATGAT TGAGTGGATG ATTGAGAAGC TGTTCCTCGT CGTGATCTC ACCCCCTCG
TTGTTTGTAG CGATGTTTAC TCCTCAAGG GAATAACTTT TACCTTACTA ACTCACTAC TAACCTCTCG ACAAGGCAC GCACTAGGAG TGGGGGAGC

157 N K I C Y K S G V P L I E N G M I E W M I E K L F P C V I L T P L D
801 ACTGCTCTG GAGGGAGCC AAACCTCCAG GGGCTCCG CTACCTGCCC GGCGGCCCG ATATCCAGTG GACCAACCTG GATCCAGAGC AGCTGCTGGA

TGACGAAGAC CTTCTCTCG TTTGAGGTTT CCGGAGGCG GATGACGCG CCGGGGCGC TATAGTAC CATGTTGAC CTAGGTCTCG TCGACGACCT
191 C F W E G A K L Q G G S A Y L P G R P D I Q W T N L D P E Q L L E

FIG. 1A

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901 GGAGCTGGGT CCCTTGGCT CCCTCGGGAG CTGCTAGACA AGGCACAGGT GGGCCAGGCC TAGCTGGGGC GGCCCTGTCT GCACCCTGAT
 CCTCGACCCA GGGAACTCCC GGAAGCCCTC GAGGATCTGT TCCGTGTCCA CCGGTGCCG ATGACCCCG CCGGACAGA CGTGGGACTA
 224 E L G P F A S L E G F R E L L D K A Q V G Q A Y V G R P C L H P D
 1001 GACCTCCACT GCCCACCTAG TGCCCCCAAC CATCACAGCA GGCAGGCTCC CAATGTGGCT CACGAGCTGA GTGGGGCTG CCATGGCTTC TCCCACAAAT
 CTGGAGGTGA CGGGTGGATC ACGGGGTTG GTAGTGTCTG CCGTCCGAGG GTTACACCGA GTGCTCGACT CACCCCGGAC GGTACCGAAG AGGTGTCTTA
 257 D L H C P P S A P N H H S R Q A P N V A H E L S G G C H G F S H K F
 1101 TCATGCACTG GCAGGAGGAA TTGCTGCTGG GAGGCATGGC CAGACACCCC CAAGGACAGC TGCTGAGGGC AGAGGCCCTG CAGAGCACCT TCTTGCTGAT
 AGTACGTGAC CGTCTCTCTT AACGACGACC CTCCTGTACC GTCTCTCTCG GTTCTCTCTG ACGACTCCCG TCTCCGGGAC GTCTCGTGA AGAACGACTA
 291 M H W Q E E L L L G G M A R D P Q G E L L R A E A L Q S T F L L M
 1201 GAGTCCCCGC CAGCTGTACG AGCATTTCCG GGGTGACTAT CAGACACATG ACATTGGCTG GAGTGAGGAG CAGGCACAGA CAGTGCTACA AGCCTGGCAG
 CTCAGGGGCG GTCCACATGC TCGTAAAGGC CCCACTGATA GTCTGTGTAC TGTAAACGAC CTCACTCCTC GTCCGTCTGT GTCACGATGT TCGGACCGTC
 324 S P R Q L Y E H F R G D Y Q T H D I G W S E E Q A S T V L Q A W Q
 1301 CGCGCGCTTG TGCAGCTGCC CCAGGAGGCC CTGCCTGAGA ACGCTTCCCA GCAGATCCAT GCCTTCTCCT CCACCACCTT GGATGACATC CTGCATGCGT
 GCGCGAAAC ACGTCGACCG GGTCTCCCG GACGACTCT TCGGAAGGT CGTCTAGGTA CGGAAGAGGA GTTGTGGGA CCTACTGTAG GACGTACGCA
 357 R R F V Q L A Q E A L P E N A S Q Q I H A F S S T T L D D I L H A F
 1401 TCTCTGAAGT CAGTGTGCTGCC CGTGTGGTGG GAGGTATCT GCTCATGCTG GCCTATGCC TGTGACCAT GTGTGGGTGG GACTGGCCCG AGTCCCAGGG
 AGAGACTTCA GTCACGACCG GCACACCACC CTCGATAGA CGAGTACGAC CGGATACGGA CACACTGGTA CGACGCCACC CTGACGCGGG TCAGGGTCCC
 391 S E V S A A R V V G G Y L L M L A Y A C V T M L R W D C A Q S Q G
 1501 TTCCGTGGGC CTGCGGGG TACTGCTGGT GGCCCTGGCG GTGGCCTCAG GCCTTGGGCT CTGTGCCCTG CTCGGCATCA CCTTCAATGC TGCCACTACC
 AAGGCACCCG GAACGGCCCC ATGACGACCA CCGGACCGC CACCGAGTC CGGAACCCGA GACACGGGAC GAGCCGTAGT GGAAGTTACG ACGGTGATGG
 424 S V G L A G V L L V A L A V A S G L G L C A L L G I T F N A A T T
 1601 CAGGTGCTGC CTTTCTTGGC TCTGGGAATC GCGGTGGATG ACGTATTCT GCTGGCGCAT GCCTTCACAG AGGCTCTGCC TGGCACCCCT CTCCAGGAGC
 GTCCACGACG GAAGAACCG AGACCTTAG CCGCACTTAC TGCATAAGGA CGACCGGTA CGGAAGTGT TCCGAGACCG ACCGTGGGA GAGTCTCTG
 457 Q V L P F L A L G I G V D D V F L L A H A F T E A L P G T P L Q E R
 1701 GCATGGGCGA GTGTCTGAG CGCACGGGCA CCAGTGTCTG ACTCACATCC ATCAACAACA TGGCCGCCTT CCTCATGGCT GCCCTCGTTC CCATCCCTGC
 CGTACCCGCT CACAGACGTC GCGTGCCCGT GGTACAGCA TGAGTGTAGG TAGTTGTTGT ACCGGCGGAA GGAGTACCGA CCGGAGCAAG GGTAGGAGC
 491 M G E C L Q R T G T S V V L T S I N N M A A F L M A A L V P I P A

FIG. 1B

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$\frac{5}{1146}$

2701 GCTCATCCAG ACTGAGACG CCCAGGAGCC TCTGGATTTC AGCCAGCTGA CCACAAGGAA GCTGGTGGAC AGAGAGGGAC TGATTCCACC CGAGCTCTTC
CGAGTAGGTC TGACCTCTGC GGTCTCTCGG AGACCTAAG TCGGTGCACT GGTGTTCTTT CGACCACCTG TCTCTCCCTG ACTAAGGTGG GCTCGAGAAG
824 L I Q T G D A Q E P L D F S Q L T T R K L V D R E G L I P P E L F
2801 TACATGGGC TGACCGTGTG GGTGAGCAGT GACCCCTCTGG GTCTGGCAGC CTCACAGGCC AACTTCTACC CCCACCTCC TGAATGGCTG CACGACAAAT
ATGTACCCCG ACTGGCACAC CCACTCGTCA CTGGGGGACC CAGACCGTGC GAGTGTCCGG TTGAAGATGG GGGGTGGAGG ACTTACCGAC GTGCTGTTTA
857 Y M G L T V W V S S D P L G L A A S Q A N F Y P P P P E W L H D K Y
2901 ACGACACCAC GGGGGAGAAC CTTCCGATCC CGCAGCTCA GCCCTTGGAG TTGCCCCAGT TCCCTTCTCT GCTGCGTGGC CTCAGAAGA CTGCAGACTT
TGCTGTGGTG CCCCCTCTTG GAAGCGTAGG GCGGTCTAGT CCGGAACCTC AAACGGGTCA AGGGAAGGA CGACGCACCG GAGGTCTTCT GACGTCTGAA
891 D T T G E N L R I P P A Q P L E F A Q F P F L L R G L Q K T A D F
3001 TGTGAGGCC ATCGAGGGG CCGGGCAGC ATGGCAGAG GCGGGCCAG CTGGGGTGCA CGCCTACCCC AGCGGCTCCC CCTTCTCTCT CTGGGAACAG
ACACCTCCG TAGCTCCCC GGGCCCGTCG TACGCGTCTC CGGCCGTCC GACCCACGT CGGATGGGG TCGCCGAGGG GGAAGGAGAA GACCTTGTG
924 V E A I E G A R A A C A E A G Q A G V H A Y P S G S P F L F W E Q
3101 TATCTGGGC TGCGCGCTG CTTCTCTGTC GCGTCTGCA TCCTGTCTGT GTGCACTTTC CTCTGTCTGT CTCTAACCCC TGGACGGCTG
ATAGACCCG ACGCCGGAC GAAGACGAC CGGCAGACGT AGGACGACCA CAGTGAAAG GAGCAGACAC GAGACGACGA GGAGTTGGG ACCTGCCGAC
957 Y L G L R R C F L L A V C I L L V C T F L V C A L L L L N P W T A G
3201 GCCTCATAGT GCTGGTCTG GCGATGATGA CAGTGGAACT CTTTGGTATC ATGGGTTTC TGGGCATCAA GCTGAGTGCC ATCCCGCTGG TGATCCTTGT
CGGAGTATCA CGACCAGGAC CGCTACTACT GTCACCTTGA GAAACCATAG TACCCAAAGG ACCCGTAGT CGACTCACGG TAGGGGCACC ACTAGGAACA
991 L I V L V L A M M T V E L F G I M G F L G I K L S A I P V V I L V
3301 GGCTCTGTA GGCATTGGC TTGAGTTTAC AGTCCACCTG GGTCTGGGCT TCCTGACCAAC CCAGGGCAGC CGGAACCTGC GGGCCGCCCA TGCCCTTGAG
CCGGAGACAT CCGTAACCGC AACTCAAGT TCAGGTGCAC CGAGACCCGA AGGACTGGTG GGTCCCGTGC GCCTTGGACG CCCGGCGSGT ACGGAACTC
1024 A S V G I G V E F T V H V A L G F L T T Q G S R N L R A A H A L E
3401 CACACATTG CCCCCGTGAC CGATGGGGC ATCTCCACAT TCCTGGGTCT GCTCATGCTT GCTGGTCCC ACTTTGACTT CATTGTAAGG TACTTCTTTG
GTGTGTAAC GGGGGCACTG GCTACCCCGG TAGAGGTGTA ACCACCCAGA CGAGTACGAA CGACCAAGG TGAAACTGAA GTAACATTC GTAAAGAAAC
1057 H T F A P V T D G A I S T L L G L L M L A G S H F D F I V R Y F F A
3501 CGCGCTGAC AGTCTCACG CTCCTGGGC TCCTCCATGG ACTCTGCTG CTGCTGTCTG TGCTGTCCAT CCTGGGCCCC CGCCAGAGG TGATACAGAT
GCCGCGACTG TCACGAGTGC GAGGACCCCG AGGAGGTACC TGAGCAGCAG GACGGACAG ACGACAGGTA GGACCCGGG GCGGTCTCC ACTATGTCTA
1091 A L T V L T L L G L L H G L V L L P V L L S I L G P P P E V I Q M

FIG. 1D

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3501 GTACAAGGAA AGCCACAGAGA TCCTGAGTCC ACCAGTCCA CAGGAGGCG GGCTTAGGTG GGGGCATCC TCCTCCCTGC CCCAGAGCTT TGCCAGAGTG
 CATGTTCTCT TCGGGTCTCT AGGACTCAGG TGGTCGAGGT GTCCCTCCGC CCGAATCCAC CCCCGTAGG AGGAGGACG GGGTCTCGAA ACGTCTCAC
 1124 Y K E S P E I L S P P A P Q G G G L R W G A S S S L P Q S F A R V
 3701 ACTACCTCCA TGACCGTGGC CATCCACCCA CCCCCCTGC CTGGTGCTTA CATCCATCCA GCCCCCTGATG AGCCCCCTTG GTCCCTGCT GCCACTAGCT
 TGATGGAGGT ACTGGCACCG GTAGGTGGT GGGGGGACG GACCACGAT GTAGGTAGGT CGGGGACTAC TCGGGGGAAC CAGGGACGA CCGTGATCGA
 1157 T T S M T V A I H P P P L P G A Y I H P A P D E P P W S P A A T S S
 3801 CTGGCAACCT CAGTTCAGG GGACCAAGTC CAGCCACTGG GTGAAAGAGC AGCTCAAGCA CAGAGACCAT GTGTGGGCG TGTGGGTCA CTGGAAGCA
 GACCGTTGGA GTCAAGGTCC CCGGTCCAG GTCCGTGACC CACTTCTCG TCGACTTCGT GTCTCTGGTA CACACCCCG ACACCCAGT GACCCCTCGT
 1191 G N L S S R G P G P A T G O
 3901 CTGGGTCTGG TGTAGACGC AGGACGGACC CCTGGAGGGC CTGCTGCTG CTGCTATCCC TCTCCGACC CAGCTGTCT GGGCCTCCCT GATATCGAAT
 GACCCAGACC ACAATCTGCG TCCTGCCTGG GGACCTCCCG GGACGACGAC GACGTAGGG AGAGGCTGG GTCGACAGTA CCCGGAGGGA CTATAGCTTA
~~ATTC (silent)~~
~~PKT follows, this is the 5' prime end of vector~~

4001 TCAATCGATA GAACCGAGGT GCAGTTGGAC
 AGTTAGCTAT CTTGGCTCCA CGTCAACCTG

FIG. 1E

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(SEQ ID NO: 3) e

	30	40	50	60	70
905531	GCTGGGGTGCACGCCCTACCNCAGCGGNTCCCCCTTCCTCTTCTGGGAACA				
	::: :: : *****				
hpatched	CTGGGGCTGTCCAGTTACCCCAACGGCTACCCCTTCCTCTTCTGGGAGCA				
(SEQ ID NO: 4) e	3010	3020	3030	3040	3050

	80	90	100	110	120
905531	GTATCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGCTGCATCCTGCTGG				
	*** * ***** *				
hpatched	GTACATCGGCCTCCGCCACTGGCTGCTGCTGTTTCATCAGCGTGGTGTGG				
	3060	3070	3080	3090	3100

	130	140	150	160	170
905531	TGTGCACTTTCCTCGTCTGTGCTCTGCTGCTCCTNAACCCCTGGACGGCT				

hpatched	CCTGCACATTTCCTCGTGTGCGCTGCTTCCTTCTGAACCCCTGGACGGCC				
	3110	3120	3130	3140	3150

	180	190	200	210	220
905531	GGCCTNATAGTGCTGGTCCTGGCGATGATGACAGTGGAACTCTTGGTAT				
	** *****				
hpatched	GGGATCATTTGTGATGGTCCTGGCGCTGATGACGGTCGAGCTGTTCCGGCAT				
	3160	3170	3180	3190	3200

	230	240	250
905531	CATGGGTTTNCCTGGGCATCAAGCTGAGT		

hpatched	GATGGGCCTCATCGGAATCAAGCTCAGT		
	3210	3220	3230

	80	90	100	110	120
905531	TCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGCTGCATCCTGCTGGTGT				
	::: ::: *				
hpatched	GCTGCTGCTGTTTCATCAGCGTGGTGTGGCC---TGCACATTTCCTCGTGT				
	3090	3100	3110	3120	

	130	140	150
905531	GCACTTTCCTCGTCTGTGCTCTGCTGCT		
	** * * * * * :		
hpatched	GCGCTGTCTTCCTTCTGAACCCCTGGAC		
	3130	3140	3150

FIG. 2A

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(SEQ ID NO: 5) 1326258 30 40 50 60 70
GCTGGGGTGCACGCCTACCCCAGCGGCTCCCCCTTCCTCTTCTGGAACA
::: :: : *****
hpatched CTGGGGCTGTCCAGTTACCCCAACGGCTACCCCTTCCTCTTCTGGGAGCA
3010 3020 3030 3040 3050

1326258 80 90 100 110 120
GTATCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGG
*** * ***** * * * * *
hpatched GTACATCGGCCTCCGCCACTGGCTGCTGCTTCATCAGCGTGGTGTGG
3060 3070 3080 3090 3100

1326258 130 140 150
TGTGCACTTTCCTCNTCTGTGCTCT

hpatched CCTGCACATTCTCGTGTGCGCTGT
3110 3120 3130

1326258 90 100 110 120 130
TCTGGGCCTGCGGCGCTGCTTCCTGCTGGCCGTCTGCATCCTGCTGGTGT
::: ::: * * * * *
hpatched GCTGCTGCTGTTTCATCAGCGTGGTGTGGCC---TGCACATTCTCGTGT
3090 3100 3110 3120

1326258 140 150
GCACTTTCCTCNTCTGTGCTCT
** * * * *
hpatched GCGCTGTCTTCCTTCTGAACCC
3130 3140

1326258 10 20 30 40 50
CCGGGCAGCATGCGCAGAGGCCGGCCAGGCTGGGGTGCACGCCTACCCCA

(SEQ ID NO: 6) hpatched.RC CCGGGCGGCATG--CGGAAGCGGACCACGCTGGGGGGTGGCTCAGGGGAG
710 720 730 740 750

FIG. 2B

(SEQ ID NO: 1)
(SEQ ID NO: 2)

1 MASAGNAAEPODRGGGGGCGICAPGRPAGGGRRRTGGLRRAAAPDRDYL
1 MTRSPPLREL .

PTCH
PTCH2

51 H R P S Y C D A A F A L E Q I S K G K A T G R K A P L W L R A K F Q R L L F K L G C Y I Q K N C G K
11 . P P S Y T P P . . A R T A A P O I L A G S L K A P L W L R A Y F Q G L L F S L G C G I Q R H C G K

PTCH
PTCH2

101 F L V V G L L F G A F A V G L K A A N L E T N V E L W V E V G G R V S R E L N Y T R Q K I G E E
58 V L F L G L L A F G A L A L G R M A I I E T N L E Q L W V E V G S R V S Q E L H Y T K E K L G E E

PTCH
PTCH2

151 A M F N P Q L M I Q T P K E E G A N V L T T E A L L Q H L D S A L Q A S R V H V Y M Y N R Q M K L E
108 A A Y T S Q M L I Q T A R Q E G E N I L T P E A L G L H L Q A A L T A S K V Q V S L Y G K S W D L N

PTCH
PTCH2

201 H L C Y K S G E L I T E T G Y M D Q I I E Y L Y P C L I I T P L D C F W E G A K L Q S G T A Y L L G
158 K I C Y K S G V P L I E N G M I E W M I E K L F P C V I L T P L D C F W E G A K L Q G S A Y L P G

PTCH
PTCH2

251 K P P L R W T N F D P L E F L E E L K K I N Y Q V D S W E E M L N K A E V G H G Y M D R P C L N P A
208 R P D I Q W T N L D P E Q L L E E L G P F A . S L E G F R E L L D K A Q V G Q A Y V V G R P C L H P D

PTCH
PTCH2

301 D P D C P A T A P N K N S T K P L D M A L V L N G G C H G L S R K Y M H W Q E E L I V G G T V K N S
257 D L H C P P S A P N H H S R Q A P N V A H E L S G G C H G F S H K F M H W Q E E L L L G G M A R D P

PTCH
PTCH2

351 T G K L V S A H A L Q T M F Q L M T P K Q M Y E H F K G Y E V S H . I N W N E D K A A A I L E A W
307 Q G E L L R A E A L Q S T F L L M S P R Q L Y E H F R G . D Y Q T H D J G W S E E Q A S T V L Q A W

PTCH
PTCH2

400 Q R T Y V E V V H Q S V A Q N S T K V L S F T T T L D D I L K S F S D V S V R V A S G Y L L M
356 Q R R F V Q L A Q E A L P E N A S Q Q I H A F S S T L D D I L H A F S E V S A A R V A G Y L L M

PTCH
PTCH2

FIG. 3A

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TM3

PTCH 450 L A Y A C L T M L R W D C S K S Q G A V G L A G V L L V A L S V A A G L G L C S L G S F N A A T
PTCH2 406 L A Y A C V T M L R W D C A Q S O G S V G L A G V L L V A L A V A S G L G L C A L L G T E N A A T

TM4

PTCH 500 T Q V L P F L A L G V G V D D V E L L A H A F S E T G Q N K R I P F E D R T G E C L K R T G A S V A
PTCH2 456 T Q V L P F L A L G V G V D D V E L L A H A F T E A L P G . . T P L O E R M G E C L Q R T G T S V V

TM5

PTCH 550 L T S I S N V T A F F M A A L I P I P A L R A F S L Q A A V V V F N F A M V L L I F P A L S M D
PTCH2 504 L T S I N N M A A F L M A A L V P P A L R A F S L Q A A V V G G T E V A V M L V F P A L L S L D

TM6

PTCH 600 L Y R R E D R R L D I F C C F T S P C V S R V I Q V E P Q A Y T D T H D N T R Y S P P P P Y S S H S
PTCH2 554 L R R R H C Q R L D V L C C F S S P C S A Q V I Q I L P Q E L G D G T V P V G

PTCH 650 F A H E T Q I T M Q S T V Q L R T E Y D P H T H V Y T T A E P R S E I S V Q P V T V T Q D T L S C
PTCH2 593 I A H L T A T V Q A F I T H C E A S S Q H V V I I L P P Q A H L V P P P S D P L G S

PTCH 700 Q S P E S T S T R D L L S Q F S D S S L H . . C L E P P C T K W T L S S F A E K H Y A P F L L K P
PTCH2 634 E L F S P G G S T R D L L G Q E E E T R Q K A A C K S L P C A R W N L A H F A R Y Q F A P L L L Q S

TM7

PTCH 748 K A K V V I F L F L G L L G V S L Y G T T R V R D G L D L T D I V P R E T R E Y D F I A A Q F K Y
PTCH2 684 H A K A V L V L F G A L L G L S L Y G A T L V Q D G L A L T D V V P R G T K E H A F L S A Q L R Y

PTCH 798 F S F Y N M Y I V T Q K A . D Y P N I Q H L L Y D L H R S F S N V K Y V M L E E N K Q L P K M W L H
PTCH2 734 F S L Y E V A L V T Q G G F D Y A H S Q R A L F D L H Q R F S S L K A V L P P P A T Q A P R T W L H

FIG. 3B

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PTCH 847 YFRQWLQGLQDAFDSQWETGKTI MPNNYKNGSDDGVLAYKLLVQTGSRDKP
 PTCH2 784 YYRNWLQGIQAADFQDQWASGRJTRHSYRNGSE DGA LAYKLLIQTGDAQEP

PTCH 897 IDISQLTKQRLVDADGIIINPSAFYIYLTAWVSNDPVA YAASQANIRPHRP
 PTCH2 834 LDFSQLTTRKLLVDREGLLJPPPELFYMG LTI V WVS SDPLGLAASQANFYPPPP

PTCH 947 EWVHDKADYMPETRLRIPAAEPIEYAOFPFYLNGLRDTSDFVEAIEKVRT
 PTCH2 884 EWLHDKYD.TTGENLRIPPAQPLEEFAOFPFLRLGLQKTA DFVEAIEGAR A

TM8

PTCH 997 ICSNYTSLGLSSYPNGYYPFLFWEQYI GLRHWL LLLFISVVLA CTFLVCAV F
 PTCH2 933 ACAEAGQAGVHAYPSGSPFLFWEQYI GLRRCFLLAVCILLVCTFLVCA L

TM9

PTCH 1047 L LNPWTAGIITVMVLA LMTVELFCMMGLI GIKLSA VPPVILLASVGIGVEF
 PTCH2 983 L LNPWTAGLIVLVLA MMTVELFCMMGLI GIKLSA IIPVVILV ASVGIGVEF

TM10

TM11

PTCH 1097 TVHVALAFLT AIGDKNRRRAVLALAHMFA PVLDGA VSTLLGV LMLAGSEFD
 PTCH2 1033 TVHVALGFLT TOGSRNLRRAHALEHTFA PVTDGAISTLLGL LMLAGSHFD

TM12

PTCH 1147 FIVRYFFA VLA I LTL LGV L NGLVLLPVLLS FFGPIYPEV SPANGLNRLPTP
 PTCH2 1083 FIVRYFFA ALTV LTL LGV L NGLVLLPVLLS ILGPPPEV IOMYKESPEILS

PTCH 1197 SP EPPPSVVR FAMP PGH THSGSDSSDSEYSSOTTVSGL SEELRH YEAOQG
 PTCH2 1133 PPAP QGGGLRWGASSSLPQS.FARVTTSM TVAIHP PPLPGAYIHPAPDEP

FIG. 3C

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PTCH 1247 AGGPAHQVIVEATENPVFAHSTVVHPESRRHPPSNPRQQPHLDSGSLPPG
PTCH2 1182 PWSPAATSSGNLSSRGPGPATG
PTCH 1297 RQQQPRRDPPREGLWPPLYRPRRDAFEISTEGHSGPSNRARWGPRGARS
PTCH 1347 HNPRNPASTAMGSSVPGYCQPIITTTASASVTAVHPPPPVPGPGRNPRGG
PTCH 1397 LCPGYPETDHGLFEDPHVPFHVRCERRDSKVEVIELQDVECEERPRGSSS
PTCH 1447 N

FIG. 3D

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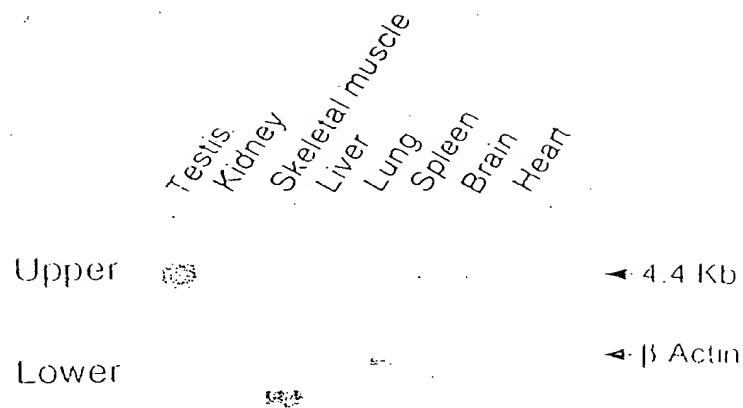


FIG. 4

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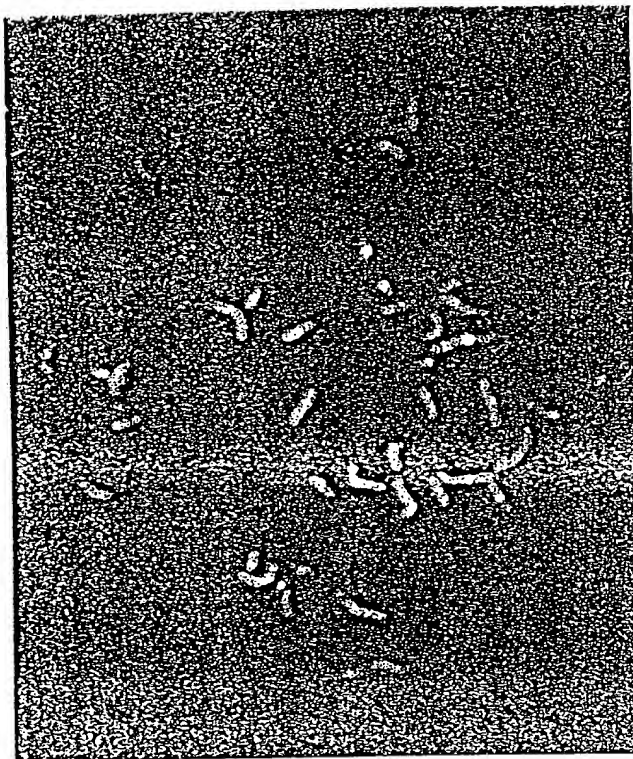


FIG. 5

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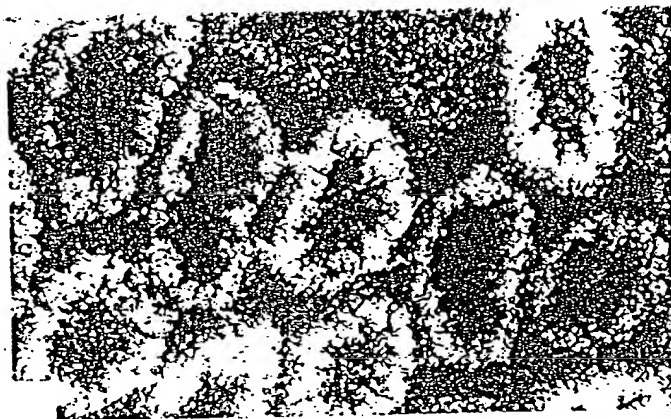


FIG. 6C

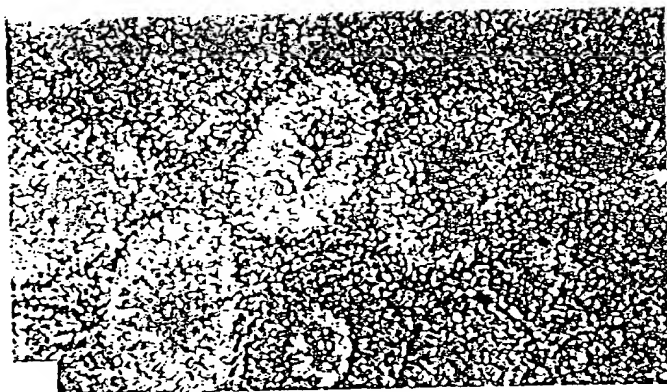


FIG. 6B



FIG. 6A

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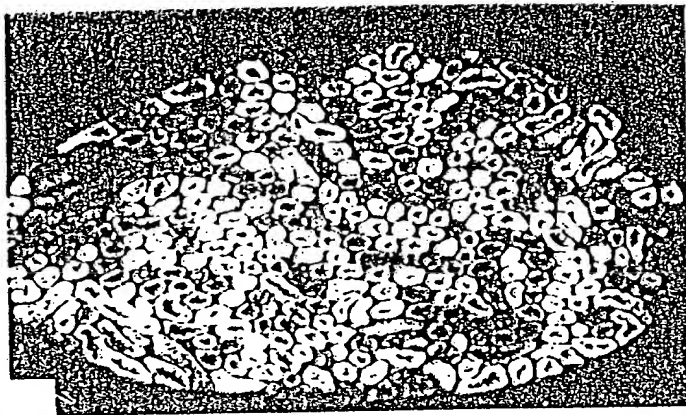


FIG. 6F

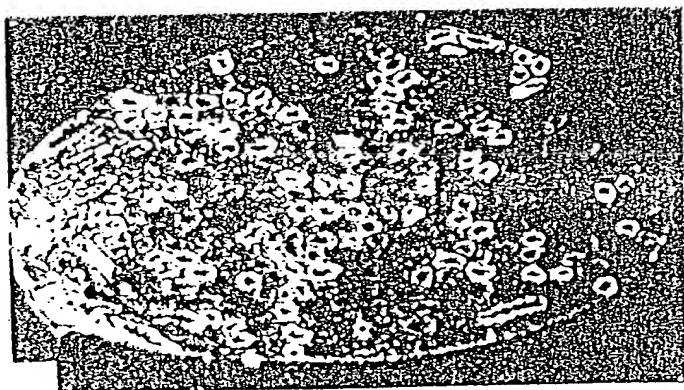


FIG. 6E

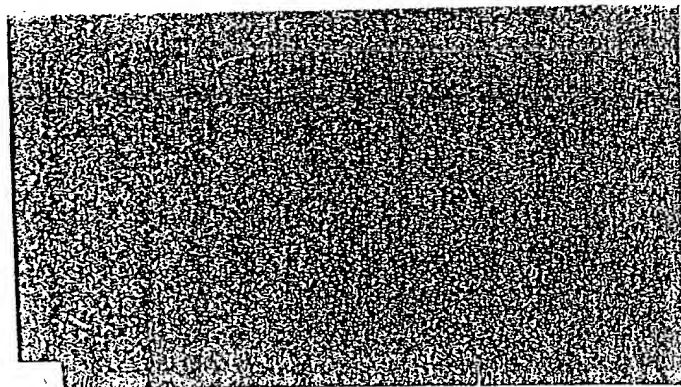


FIG. 6D

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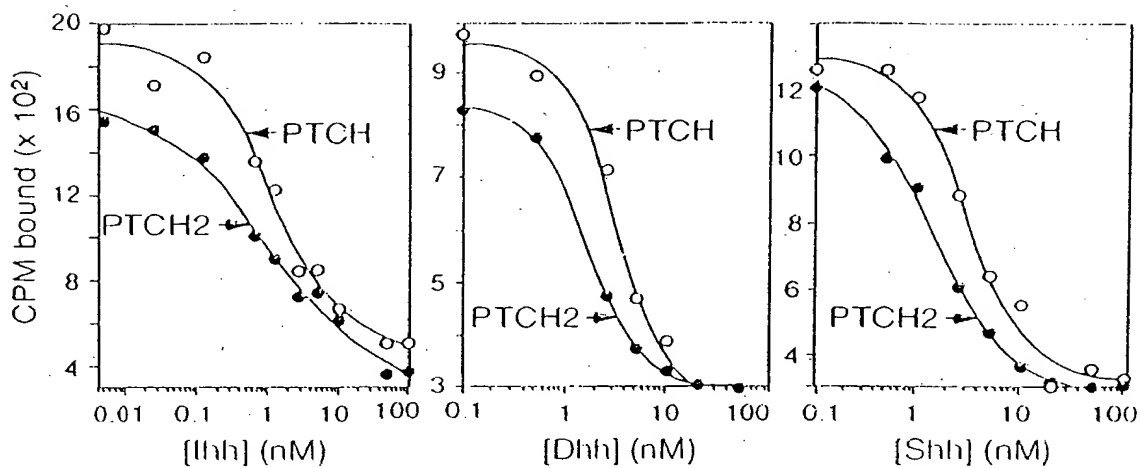


FIG. 7A

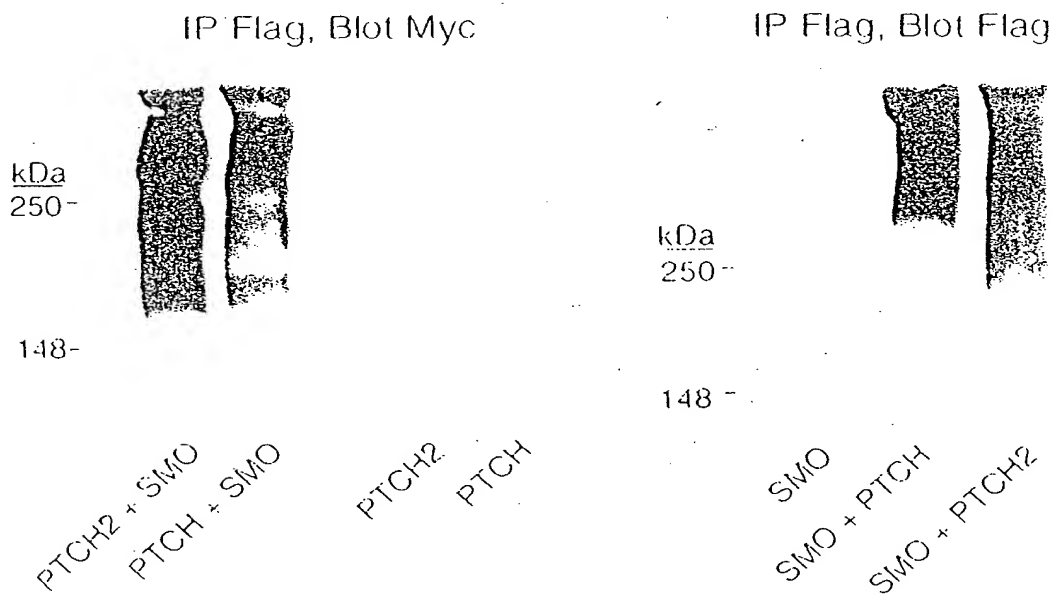


FIG. 7B

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	10	20	30	40	50
<i>hPtch-2</i>	MTRSPPLRELPPSYTPPARTAAPQILAGSLKAPLWLRAYFQGLLFSLGCG				
	* * * * *				
<i>mPatched2</i>	MVRPLSLGELPPSYTPPARSSAPHILAGSLQAPLWLRAYFQGLLFSLGCR				
(SEQ ID NO: 7)	10	20	30	40	50
	60	70	80	90	100
<i>hPtch-2</i>	IQRHCGKVLFLGLLAFGALALGLRMAIIETNLEQLWVEVGSRVSQELHYT				
	* * * * *				
<i>mPatched2</i>	IQKHCGKVLFLGLVAFGALALGLRVAVIETDLEQLWVEVGSRVSQELHYT				
	60	70	80	90	100
	110	120	130	140	150
<i>hPtch-2</i>	KEKLGEEAAYTSQMLIQATARQEGENILTPEALGLHLQAALTASKVQVSLY				
	* * * * *				
<i>mPatched2</i>	KEKLGEEAAYTSQMLIQTAHQEGGNVLTPEALDLHLQAALTASKVQVSLY				
	110	120	130	140	150
	160	170	180	190	200
<i>hPtch-2</i>	GKSWDLNKICYKSGVPLIENGMIIEWMIEKLFPCVILTPLD CFWEGAKLQG				
	* * * * *				
<i>mPatched2</i>	GKSWDLNKICYKSGVPLIENGMIERMIEKLFPCVILTPLD CFWEGAKLQG				
	160	170	180	190	200
	210	220	230	240	250
<i>hPtch-2</i>	GSAYLPGRPDIQWTNLDPEQLLEELGPFASLEGFREL LDKAQVGQAYVGR				
	* * * * *				
<i>mPatched2</i>	GSAYLPGRPDIQWTNLD PQQLLEELGPFASLEGFREL LDKAQVGQAYVGR				
	210	220	230	240	250
	260	270	280	290	300
<i>hPtch-2</i>	PCLHPDDLHCPPSAPNHHSRQAPNVAHEL SGGCHGF SHKFMHWQEELLLG				
	* * * * *				
<i>mPatched2</i>	PCLDPDDPHCPPSAPNRHSRQAPNVAQEL SGGCHGF SHKFMHWQEELLLG				
	260	270	280	290	300
	310	320	330	340	350
<i>hPtch-2</i>	GMARDPQGELLRAEALQSTFLLMSPRQLYEHFRGDYQTHDIGWSEEQAST				
	* * * * *				
<i>mPatched2</i>	GTARDLQGQLLRAEALQSTFLLMSPRQLYEHFRGDYQTHDIGWSEEQASM				
	310	320	330	340	350

FIG. 8A

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	360	370	380	390	400
<i>hPtc-2</i>	VLQAWQRRFVQLAQEALPENASQQIHAFSSTTLDDILHAFSEVSAARVVG				

<i>mPatched2</i>	VLQAWQRRFVQLAQEALPANASQQIHAFSSTTLDDILRAFSEVSTTRVVG				
	360	370	380	390	400
	410	420	430	440	450
<i>hPtc-2</i>	GYLLMLAYACVTMLRWDCAQSQGSVGLAGVLLVALAVASGLGLCALLGIT				

<i>mPatched2</i>	GYLLMLAYACVTMLRWDCAQSGAVGLAGVLLVALAVASGLGLCALLGIT				
	410	420	430	440	450
	460	470	480	490	500
<i>hPtc-2</i>	FNAATTQVLPFLALGIGVDDVFLLAHAFTEALPGTPLQERMGECLQRTGT				

<i>mPatched2</i>	FNAATTQVLPFLALGIGVDDIFLLAHAF TKAPDTP LPERMGECLRSTGT				
	460	470	480	490	500
	510	520	530	540	550
<i>hPtc-2</i>	SVVLTSINNMAAFLMAALVPIPALRAFSLQAAIVVGCTFVAVMLVFPAIL				
	** *** ** ***** *				
<i>mPatched2</i>	SVALTSVNNMVAF FMAALVPIPALRAFSLQAAIVVGCNFAAVMLVFPAIL				
	510	520	530	540	550
	560	570	580	590	600
<i>hPtc-2</i>	SLDLRRRHRCQRLDVLCCFSSPCSAQVIQILPQELGDGTVPVGIAHLTATV				

<i>mPatched2</i>	SLDLRRRHRQRLDVLCCFSSPCSAQVIQMLPQELGDRAVPVGIAHLTATV				
	560	570	580	590	600
	610	620	630	640	650
<i>hPtc-2</i>	QAFTHCEASSQHVV TILPPQAH LVPPSDPLGSELFSPGGSTRDLLGQEE				

<i>mPatched2</i>	QAFTHCEASSQHVV TILPPQAH LLSPASDPLGSELYSPGGSTRDLLSQEE				
	610	620	630	640	650
	660	670	680	690	700
<i>hPtc-2</i>	ETRQKAACKSLPCARWNLAHFARYQFAPLLLQSHAKAIVLVLF GALLGLS				
	* *** * * ***** *				
<i>mPatched2</i>	GTGPQAACRP LLCAHWTLAHFARYQFAPLLLQTRAKALVLLFF GALLGLS				
	660	670	680	690	700

FIG. 8B

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	710	720	730	740	750
<i>hPtc-2</i>	LYGATLVQDGLALTDVVPRGTKEHAFLSAQLRYFSLYEVALVTQGGFDYA				

mPatched2	LYGATLVQDGLALTDVVPRGTKEHAFLSAQLRYFSLYEVALVTQGGFDYA				
	710	720	730	740	750

	760	770	780	790	800
<i>hPtc-2</i>	HSQRALFDLHQRFSCLKAVLPPPATQAPRTWLHYYRNWLQGIQAAFDQDW				

mPatched2	HSQRALFDLHQRFSCLKAVLPPPATQAPRTWLHYYRSWLQGIQAAFDQDW				
	760	770	780	790	800

	810	820	830	840	850
<i>hPtc-2</i>	ASGRITRHSYRNGSEDGALAYKLLIQTGDAQEPLDFSQLTTRKLV DREGL				

mPatched2	ASGRITRHSYRNGSEDGALAYKLLIQTGNAQEPLDFSQLTTRKLV DKEGL				
	810	820	830	840	850

	860	870	880	890	900
<i>hPtc-2</i>	IPPELFYMGLTVWVSSDPLGLAASQANFYPPPPEWLHDKYDTTGENLRIP				

mPatched2	IPPELFYMGLTVWVSSDPLGLAASQANFYPPPPEWLHDKYDTTGENLRIP				
	860	870	880	890	900

	910	920	930	940	950
<i>hPtc-2</i>	PAQPLEFAQFPFLRLGLQKTADFVEAIEGARAACAEAGQAGVHAYPSGSP				

mPatched2	AAQPLEFAQFPFLRLHGLQKTADFVEAIEGARAACTEAGQAGVHAYPSGSP				
	910	920	930	940	950

	960	970	980	990	1000
<i>hPtc-2</i>	FLFWEQYLGLRRCFLLAVCILLVCTFLVCALLLLNPWTAGLIVLVLAMMT				

mPatched2	FLFWEQYLGLRRCFLLAVCILLVCTFLVCALLLLSPWTAGLIVLVLAMMT				
	960	970	980	990	1000

	1010	1020	1030	1040	1050
<i>hPtc-2</i>	VELFGIMGFLGIKLSAIPVVILVASVGIGVEFTVHVALGFLT TQGSRNLR				

mPatched2	VELFGIMGFLGIKLSAIPVVILVASIGIGVEFTVHVALGFLT SHGSRNLR				
	1010	1020	1030	1040	1050

FIG. 8C

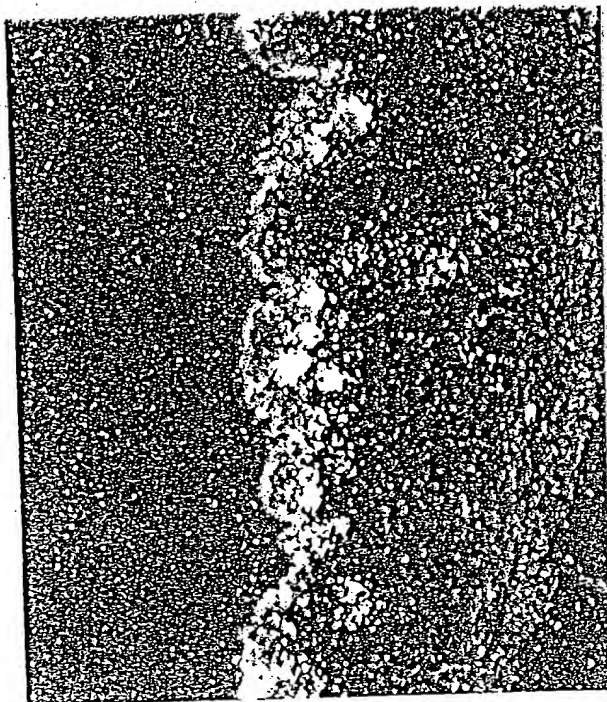
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	1060	1070	1080	1090	1100
<i>hPtch-2</i>	AAHALEHTFAPVTDGAISTLLGLLMLAGSHFDFIVRYFFAALTVLTLGL				
	** ***.*****.*****.*****.*****.*****				
<i>mPatched2</i>	AASALEQTFAPVTDGAVSTLLGLLMLAGSNFDFIIRYFFVVLTVLTLGL				
	1060	1070	1080	1090	1100
	1110	1120	1130	1140	1150
<i>hPtch-2</i>	LHGLVLLPVLLSILGPPPEVIQMYKESPEILSPPAPQGGGLRWGASSSLP				
	****.*****.*.*.*****.*...***.*****...*				
<i>mPatched2</i>	LHGLLLLPVLLSILGPPPQVVQVYKESPQTLNSAAPQRGGLRWDRPPTLP				
	1110	1120	1130	1140	1150
	1160	1170	1180	1190	1200
<i>hPtch-2</i>	QSFARVTTSMTVAIHPPPLPGAYIHPAPDEPPWSPAATSSGNLSSRGPGP				
	*****.*****.***...				
<i>mPatched2</i>	QSFARVTTSMTVALHPPPLPGAYVHPASEEPT				
	1160	1170	1180		
<i>hPtch-2</i>	ATG				

FIG. 8D

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PTCH2



PTCH

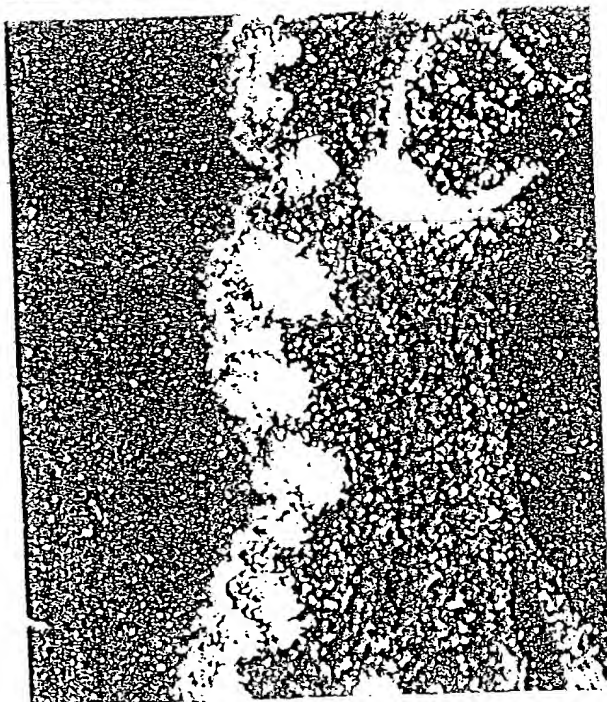


FIG. 9

~~Consensus sequence of human patched-2 cDNA clone~~
~~length: 1004 bp~~

(SEQ ID NO: 8)

1 CCCACGCGTC CGGAGAAGC TGGGGGAGGA GGTGTCATAC ACCTCTCAGA TGCTGATACA GACCGCACGC CAGGAGGGAG AGAATATCCT CACACCGGAA
GGGTGCGCAG GCCCTCTTCG ACCCCCTCCT CCGACGTATG TGGAGAGTCT ACGACTATGT CTGGCGTGCG GTCCTCCCTC TCTTGTAGGA GTGTGGGCTT

101 GCACCTTGCC TCCACCTCCA GGCAGCCCTC ACTGCCAGTA AAGTCCAAGT ATCACTCTAT GGGAGTCTCT GGGATTGAA CAAATCTGC TACAAGTCAG
CGTGAACCGG AGGTGGAGGT CCGTCGGGAG TGACGGTTCAT TTCAGGTTCA TAGTGAGATA CCTTTCAGGA CCTTAACTT GTTTTAGAGG ATGTTCAAGT

201 GAGTTCCTCT TATTGAAAT GGAATGATTG AGCGGATGAT TGAGAAGCTG TTTCCGTGCG TGATCCTCAC CCCCCTCGAC TGCTTCTGGG AGGAGGCCAA
CTCAAGGGGA ATAACTTTTA CCTTACTAAC TCGCCTACTA ACTCTTCGAC AAAGGCACGC ACTAGGAGTG GGGGAGCTG AGGAAGACCC TCCCTCGGTT

301 ACTCCAAGGG GGCTCCGCCT ACCTGCCGCT CCCAATGAG CTCACGAGCT GAGTGGGGC TGCCATGCT TCTCCACAA ATTCAATGCAC TGGCAGGAGG
TGAGGTTCCC CCGAGGCGA TGGACGGCGA GGGTTACACC GATGCTCTGA CTCACCCCG ACGGTACCGA AGAGGGTGT TAAGTACGTG ACCGTCTCTC

401 AATTGCTGCT GGGAGGCATG GCCAGAGACC CCCAAGGAGA GCTGTGAGG GCAGAGGCC TGCAGAGCAC CTTCTTGCTG ATGAGTCCCC GCCAGCTGTA
TTAACGACGA CCTCTCGTAC CCGTCTCTG GGGTTCTCT CGACGACTCC CGTCTCCGG ACGTCTCGTG GAAGAAGCAC TACTCAGGG CCGTCCGACAT

501 CGAGCATTC CCGGGTGACT ATCAGACACA TGACATTGGC TGGAGTGAGG AGCAGGCCAG CACAGTGCTA CAAGCCTGGC AGCGCGCTT TGTGCAGGTC
GCTCGTAAAG GCCCCACTGA TAGTCTGTGT ACTGTAAACG ACCTCACTCC TCGTCCGGTC GTGTACGAT GTTCGGACCG TCGCCCGCAA ACAGTCCAG

601 GGTATGGACA AGGACAGGGG GGTGCCCTGA GGCCATTCCC TCCTCCTGCC CCCTCCTATC CACCTGTCTT CTCCAGCTGG CCCAGGAGGC CTTGCCCTGAG
CCATACCTGT TCTGTGTCCT CCACGGGACT CCGGTAAGG AGGAGGACGG GGGAGGATAG GTGGGACAAA GAGGTCCGACC GGTCTCTCCG GGACGGACTC

701 AACGTTTCCC AGCAGATCCA TGCTTCTCTC TCCACCACC TGGATGACAT CCTGCATGCG TTCTCTGAAG TCAGTGTGTC CCGTGTGGTG GGAGGCTATC
TTGCCAAGGG TCGTCTAGGT ACGGAAGAGG AGGTGGTGGG ACCTACTGTA GGACGTACCG AAGAGACTTC AGTCAGGAGG GGCACACCAC CCTCCGATAG

801 TGCTATGGT GGTCTTTGCA CTGGGCACCT TGCCCCCACC CCACCTCCA CCAGTCCCCA CCTGGGGAG CCCCTGAGAC TGCCCTTTTCC CCCCACAGCT
ACGAGTACCA CCCACAACGT GGACCGTGA ACGGGGGTGG GGTGGAGGTT GGTACCGGT GGGACCCCTC GGGGACTCTG ACGGGAAGG GGGGTGTCGA

FIG. 10A

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901 GGCCTATGCC TGTGTGACCA TGCTGCGGTG GGACTGGGCC CAGTCCAGG GTTCCGTGGG CTTGGCCGG GTACTCTGG TGGCCCTGGC GTGGCCTCA
CCGGATACGG ACACACTGGT ACGACGCCAC CCTGACGCGG GTCAGGCTCC CAAGGCACCC GGAACGGCCC CATGACGACC ACCGGGACCG CCACCGGAGT

1001 GGCCTTGGGC TCTGTGCCCT GCTCGGCATC ACCTTCAATG CTGCCACTAC CCAGGTACGC CAGGACTGCA GGCAGACTC AGTCCAGTC ACCAGGCTTC
CCGGAACCCG AGACACGGGA CGAGCCGTAG TGAAGTTAC GACGGTGATG GGTCATGCG GTCCTGACGT CCCGTCTGAG TCACGCTCAG TGGTCCGAAG

1101 ACGGCTCTC AGCTGCCCGC TCCTCTGCC CTCCAGGTGC TGGCCCTCTT GACTCTGGGA ATCGGCGTGG ATGACGTATT CCTGTGGCG CATGCCCTCA
TGCCCAGGAG TCGACGGCG AGGACACGG GAGGTCCACG ACGGGAAGAA CTGACACCTT TAGCCGCACC TACTGCATAA GGACGACCGC GTACGGAAGT

1201 CAGAGGCTCT GCCTGGCACC CCTCTCCAGG TGGGGCCCTG TCCCCACAGG CTCTCTGAG GCAGCTCACC TTACTGTTA AGAGCTCTT GGTCAAGTG
GTCTCCGAGA CCGACCGTGG GGAGAGTCC ACCCCGGAAC AGGGGTCCC GATAGACTC CGTCAGTCC AATGACCAAT TCTCGAGAA CCAAGTTCC

1301 ACCTTGGGCT GCTAATGAAC CTCGGTGCCT CTTGTCCCA TGTGTAAACA GGGAAATAA TAGTGCTGTG TCCTAAGGGT TATTGTTGG ATCAGTGAAG
TGGAAACCCGA CGATTACTTG GAGCCACGGA GAACAGGGT ACACATTTGT CCCCTTATT ATCACGACAC AGGATTCCCA ATAACAACC TAGTCACTTC

1401 TAACTCAAGT TGAATGTTA GAACAGCCCA TCATACGTAC ATGGTACCCA ATAAATGCTA GCCACTGTGT TATGACTGCC CCACCTCTGC ACCCAAGTT
ATTGAGTTCA ACTTACGAAT CTTGTGCGGT AGTATGCATG TACCATGGGT TATTACCAT CGGTGACACA ATACTGACCG GGTGGAGACG TGGGGTTCAA

1501 CCTGAGCCTC CCCTTCACTC CACTTTGACA CGGCCCTCC CTTGTGACCT GAGGGCAGGT CCCCACTCTG TCCTGGCAGG AGCGCATGGG CGAGTGTCTG
GGACTCGGAG GGAAGTGAG GTGAATGT GCGCGGAGG GAACACTGGA CTCCCTTCCA GGGGTGAGAC AGGACCGTCC TCGCGTACCC GCTCACAGAC

1601 CAGCGCACGG GCACCACTGT TGTACTCACA TCCATCAACA ACATGGCCGC CTTCTCTCATG GCTGCCCTCG TTCCCATCCC TGGCGTGGCA GCCTTCTCCC
GTCCGCTGCC CGTGGTCACA ACATGAGTGT AGGTAGTGT TGTACCGGCG GAAGGAGTAC CGACCGGAGC AAGGGTAGGG ACGCGACGCT CGGAAGAGGG

1701 TACAGCCTGG ACCTACGGG GCGCCACTGC CAGCGCCTTG ATGTGCTCTG CTGCTTCTCC AGTACTGCC TGGCCCCCAG CCCCTTCTC CCGTGACCCA
ATGTCGGACC TGGATGCCGC CGCGGTGACG GTCGCGGAAC TACACGAGAC GACGAAGAGG TCCATACGG ACGCGGGTTC GGGGAAGGAG GGCACCTGGT

1801 CGCCAGCCTG TCCCTCACC AGCATTTCAA AGCATTTCAA GGCACAGACC TGTCTACCTC TCTCTACCTC TTCCAGTCCC TGCTCTGCTC AGTGTATTCA GATCCTGCC
GCGGTGGAC AGGGGAGTGG TCGTAAAGTT CCGTGTCTGG ACAGTAGGTG AGAGATGGAG AAGGTACGGG ACGAGACGAG TCCACTAAGT CTAGGACGGG

1901 CAGGAGCTGG GGAACGGGAC AGTACCAGTG GGCATTGCC ACCTACTGC CACAGTTCAA GCCTTTACCC ACTGTGAAGC CAGCAGCCAG CATGTGGTCA
GTCTCGACC CCCTGCCCTG TCATGGTCA CCGTAACGGG TGGAGTGACG GTGTCAAGTT CGGAATGGG TGACACTTCG GTCGTGGTTC GTACACCAGT

2001 CCATCTCTGCC TCCCAAGCC CACCTGGTGC CCCCACCTTC TGACCCACTG GGCTCTGAGC TCTTCAGCCC TGGAGGTCC ACACGGGACC TTCTAGGCCA
GGTAGGACGG AGGGTTCCG GTGGACCACG GGGGTGGAAG ACTGGGTGAC CCGAGACTCG AGAAGTCCGG ACCTCCAGG TGTGCCCTGG AAGATCCGGT

FIG. 10B

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2101 GGAGGAGGAG ACAAGGCAGA AGGCAGCCTG CAAGTCCCTG CCTGTGCCC GCTGGAATCT TGCCCATTTT GCCCGCTATC AGTTTGCCCC GTTGCTGCTC
CCTCCTCCTC TGTTCCTCT TCCGTCCGAC GTTCAGGGAC GGGACACGGG CGACTTTAGA ACGGGTAAAG CCGGCGATAG TCAAACGGGG CAACGACGAG

2201 CAGTCACATG CCAAGGCCAT CGTCTGGTG CTCTTTGGTG CTCTTCTGGG CCTGAGCCTC TACGGAGCCA CCTTGGTGCA AGACGGCCTG GCCCTGACGG
GTCAGTGATC GGTTCGGTA GCACGACCAC GAGAAACCAC GAGAAGACCC GGAATCGGAG ATGCCTCGGT GGAACCACTT TCTGCCGGAC CGGACTGCC

2301 ATGTGGTGCC TCGGGGACAC AAGGAGCATG CCTTCCTGAG CGCCCAGCTC AGTACTTCT CCCTGTACGA GGTGGCCCTG GTGACCCAGG GTGGCTTTGA
TACACCACGG AGCCCGGTGG TTCTCTGTAC GGAAGGACTC GCGGGTCGAG TCCATGAAGA GGGACATGCT CCACCGGAC CACTGGGTCC CACCGAAACT

2401 CTACGCCCCAC TCCCAACGGG CCTCTTTTGA TCTGCACCAG CGCTTCAGTT CCCTCAAGGC GGTGCTGCC CCACCGGCCA CCCAGGGACC CCGACCTGG
GATCGGGTG AGGTTGCGC GGGAGAAACT AGACGTGGTC GCGAAGTCAA GGGAGTCCG CCACGACGGG GGTGGCCGGT GGTCCGTGG GCGTGGACC

2501 CTGCACTATT ACCGCAACTG GCTACAGGGA ATCCAGGCTG CCTTTGACCA GGAATGGGT TCTGGGGCCA TCACCCGGCA CTCGTACCGC AATGGCTCTG
GACGTGATAA TGGCGTTGAC CGATGTCCTT TAGGTCCGAC GGAACCTGGT CCTGACCCGA AGACCCGGT AGTGGCGGT GAGCATGGCG TTACCGAGAC

2601 AGGATGGGGC CCTGGCCTAC AAGCTGCTCA TCCAGACTGG AGACGCCAG GAGCCTCTGG ATTTACAGCCA GGTGGGAGA GGGCTGGAGG GGTCCACTAG
TCTACCCCG GGACCGGATG TTCGACGAGT AGGTCTGACC TCTCGGGTC CTCGGAGACC TAAAGTCGGT CCAACCCCTCT CCCGACCTCC CCAGGTGATC

2701 TACAGGGGCT GCAGGCCTCC TGGGCCCAGG CCTTCAGCCC TCTCTGCCCTC TGCAGCTGAC CACAAGGAAG CTGGTGGACA GAGAGGGACT GATTCCACCC
ATGTCCCCGA CGTCCGGAG ACCCGGGTCC GGAAGTCGGG AGACACGGAG ACGTCGACTG GTGTTCTTTC GACCACCTGT CTCTCCCTGA CTAAGGTGGG

2801 GAGTCTTCT ACATGGGGCT GACCGTGTGG GTGAGCAGTG ACCCCCTGGG TCTGGCAGCC TCACAGGCCA ACTTCTACCC CCCACCTCCT GAATGGCTGC
CTCGAGAAGA TGTACCCCGA CTGGCACACC CACTCGTCAC TGGGGACCC AGACCGTCCG AGTGTCGGT TGAAGATGGG GGGTGGAGGA CTTACCGAGC

2901 ACGACAAATA CGACACCACG GGGGAGAAC TTGCGCAGTGA GTCTTGGGGG GAGCTCGGA AGAGCCTCAG CCTCGCCAC ACAAGCCCTG AGCCTGAGGC
TGCTGTTTAT GCTGTGGTGC CCCCTCTTGG AAGCGTCACT CAGAACCCCT CTCGAGCCCT TCTCGAGTC GAGCGGGTG TGTTCGGAC TCGGACTCCG

3001 CCTGCCCACT CTGCCCGGTG CTCACCGCCC TGTCCCTCTC CCTCTTCTCC CTTCACAGT CCGGCCAGCT CAGCCCTGG AGTTTGCCCA
GGACGGGTGA GACGGGGCAC GAGTGGCGG ACAGGGAGAG GGAGAGAGG GAAGGGGAGG GGAGGTGTC GGGCGGTGCA GTCGGGAACC TCAAACGGGT

FIG. 10C

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3101 GTTCCCTTC CTGCTGCGTG GCCTCCAGAA GACTGCAGAC TTTGTGGAGG CCATCGAGGG GGCCCGGGCA GCATGCGCAG AGCCCGGCCA GGCTGGGGTG
CAAGGGGAAG GACGACGCAC CGGAGGTCTT CTGACGTCTG AACACCTCC GGTAGTCCC CCGGGCCCGT CGTACGCGTC TCCGGCCCGT CCGACCCAC
3201 CACGCCCTACC CCAGCGGCTC CCCCTTCCTC TTCTGGGAAC AGTATCTGGG CCTGCGGCGC TGCTTCCTGC TGGCCGCTCG CATCTGCTG GTGTGCACTT
GTGCGGATGG GGTGCGCGAG GGGGAAGGAG AAGACCCTTG TCATAGACCC GGACGCGCG ACAGAGGACG ACCGGCAGAC GTAGGACGAC CACACGTGAA
3301 TCCTCGTCTG TGCTCTGCTG CTCCTCAACC CCTGACGGC TGCCCTCATA GTGAGTGCTT GCAGGAGTG GGACAGAGAC ACCCCACCTT TCCCTGCCCA
AGGAGCAGAC ACAGACGCAC GAGGAGTTGG GGACTGCGG ACCGGAGTAT CACTACGAA CGTCTCACC CCGTCTCTG TGGGGTGGGA AGGACCGGT
3401 GCCTGTGATC CCTCCTGCCA GGAGCCCTCT GTGAGCCCTG TCTCCCTCAG GTGCTGGTCC TGGCGATGAT GACAGTGGAA CTCTTTGTA TCATGGGTTT
CGACAGTAG GGAGGACGGT CCTCGGAGA CACTCGGGAC AGAGGGAGTC CACGACCAGG ACCGCTACTA CTGTCACTT GAGAAACCAT AGTACCCAAA
3501 CTGGGGCATC AAGCTGAGTG CCATCCCGGT GGTGATCCTT GTGGCCTCTG TAGGCATTGG CGTTGAGTTC ACAGTCCACG TGGCTCTGCT GAGCACGGGC
GGACCCGTAG TTCGACTCAC GGTAGGGCA CCACTAGGAA CACCGGAGAC ATCCGTAACC GCAACTCAAG TGTCAGGTGC ACCGAGACCA CTCGTGCCCG
3601 ACCCGGGGA GGGACCAATC AGCTGATTCA GTATTCAACA CATATTGTTT AAGCCCTAC TATGTGCTAG GTACTATTTA AGAATTGGG CTGGGTGGAC
TGGGCCCTT CCTGGTTAG TCGACTAAGT CATAAGTTGT GTATAACAAG TTCGGGGATG ATACACGATC CATGATAAAT TCTTAAACCC GACCCACCTG
3701 GTGGTGGCTC ATTCTGTAA TCCCAGCACT TTGGGAGGCC GAGGCGGGTG GATCACCTGA GGTCGGGAGT TCGAAACCAG CCTGGCCAC ATGGTGAAAC
CACCAACCGAG TAAGGACATT AGGTCTGTGA AACCTCCGG CTCGCCCCAC CTAGTGGACT CCAGCCCTCA AGCTTGGTC GGACCGGTTG TACCACCTTG
3801 CCTGTCTTTA CTAAAAATAC AAAAAATTAG CCAGGCGTGG TGGACATGC CAGTAGTCCC AGCTACTTTG GAGGTGAGG CAGAATTGCT TGAACCTGGG
GGACAGAAAT GATTTTATG TTTTITATC GGTCCGCACC ACCGTGTACG GTCATCAGGG TCGATGAAAC CTCGACTCC GTCTTAACGA ACTTGGACCC
3901 AGGCGAAGGT TGCAGTGAGC TGAGATCGTG CCATTGCACT CCAGCCTGGG CAACAAGAGT GCAACTCTCC GTCTCAAAA AAAAAAAA AAGGGCGGCC
TCCGCTTCCA ACCTCACTCG ACTCTAGCAC GGTACGTTGA GGTGCGACCC GTGTCTCTCA CGTTGAGAGG CAGAGTTTTT TTTTTTTTTT TTCCCGCCGG

4001 GCGA
CGCT

FIG. 10D

~~clone 16-1 human patched 2~~
~~length 2002 bp~~

(SEQ ID NO: 9)

1 TTCCGGCATG ACTCGATCGC GCGCCCTCAG AGAGCTGCC CCGAGTTACA CACCCCCAGC TCGAACCGCA GCACCCACAG TCCTACTGG GAGCCTGAAG
AAGCCGTAC TGAGCTAGCG CCGGGAGTC TCTCGACGG GGCTCAATGT GTGGGGTGC AGCTTGGCGT CGTGGGTCT AGGATCGACC CTCGACTTC

101 GCTCCACTCT GGCTTCGTGC TTACTTCCAG GGCCTGCTCT TCTCTCTGG ATGGGGATC CAGAGACATT GTGGCAAAGT GCTCTTTCTG GACTGTGTTGG
CGAGGTGAGA CCGAAGCAG AATGAAGTC CCGGACGAGA AGAGAGACCC TACGCCCTAG GTCTCTGTAA CACCGTTTCA CGAGAAAGAC CCTGACAACC

201 CCTTTGGGC CCTGGCATTG GGTCTCCGCA TGGCCATTAT TGAGACAAAC TTGGAAACAG TCTGGGTAGA AGTGGGCAGC CGGGTGAGCC AGGAGCTGCA
GGAAACCCCG GGACCGTAAT CCAGAGCGCT ACCGGTAATA ACTCTGTTTG AACCTGTGCG AGACCCATCT TCACCCGTCG GCCCACTCGG TCCTCGACGT

301 TTACACCAAG GAGAAGCTGG GGGAGGAGGC TGCATACACC TCTCAGATGC TGATACAGAC CGCACGCCAG GAGGGAGAGA ACATCCTCAC ACCCGAAGCA
AATGTGGTTC CTCCTCGACC CCTCCTCCG ACGTATGTGG AGAGTCTACG ACTATGCTCG GCGTGGGTC CTCCTCTCTT TGTAGGAGTG TGGGCTTCGT

401 CTTGGGCTCC ACCTCCAGGC AGCCCTCACT GGCAGTAAAG TCCAAAGTATC ACTCTATGG AGTCTCTGG ATTTGAACAA AATCTGCTAC AAGTCAGGAG
GAACCGGAG TGGAGGTCCG TCGGGAGTGA CCGTCAATTC AGGTTTCATAG TGAGATACCC TTCAGGACCC TAAACTTGTT TTAGACGATG TTCAGTCTCTC

501 TTCCCTTAT TGAAATGGA ATGATTGAGT GGATGATTGA GAAGCTGTTT CCGTGGGTGA TCTTCACCC CCTCGACTGC TTCTGGGAGG GAGCCAAACT
AAGGGGATA ACTTTTACCT TACTAACTCA CCTACTAACT CTTCGACAAA GGCACGCACT AGGAGTGGGG GGAGCTGACG AAGACCTCC CTCGGTTTGA

601 CCAAGGGGGC TCCGCTTACC TGCCCGGGCG CCGGATATC CAGTGGACCA ACCTGGATCC AGAGCAGCTG CTGGAGGAGC TGGGTCCCTT TGCCTCCCTT
GGTTCCCGCG AGGCGGATGG ACGGCGCGCG GGGCCTATAG GTCACCTGGT TGGACCTAGG TCTCGTCGAC GACCTCCTCG ACCCAGGGAA ACGGAGGGAA

701 GAGGGCTTCC GGGAGCTGCT AGACAAGGCA CAGGTGGGCC AGGCTTACGT GGGCGGGCCC TGCTGTCACC CTGATGACCT CCACTGCCCA CCTAGTGCCC
CTCCCGAAG CCCTCGACGA TCTGTTCCGT GTCCACCCCG TCCGGATGCA CCGCGGGGG ACAGACGTGG GACTACTGGA GGTGACGGGT GGATCACGGG

801 CCAACCATCA CAGCAGGCGC GTTCCCAATG TGGCTCACGA GCTGAGTGG GGCTGCCATG GCTTCTCCCA CAAATTCATG CACTGGCAGG AGGAATTGCT
GGTTGGTAGT GTCGTCCGTC CGAGGGTTAC ACCAGTGCT CCACTCACCC CCGACCGTAC CGAAGAGGGT GTTTAAGTAC GTGACCGTCC TCCTTAACGA

901 GCTGGGAGC ATGGCCAGAG ACCCCCAAGG AGAGCTGCTG AGGCGAGAG CCCTGCAGAG CACTTCTTG CTGATGAGTC CCCGCCAGCT GTACGAGCAT
CGACCCCTCG TACCGGTCTC TGGGGTTCC TCTCGACGAC TCCGCTCTCC GGGACGTCTC GTGGAAGAAC GACTACTCAG GGGCGGTGCA CATGCTCGTA

FIG. 11A

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1001 TTCCGGGGTG ACTATACAGAC ACATGACATT GGCTGGAGTG AGAGCAGGC CAGCACAGTG CTACAAGCCT GGCAGCGGCG CTTTGTGCAG CTGGCCCCAGG
AAGGCCCCAC TGATAGTGTG TGTAAGTGTAA CCGACCTCAC TCCTCGTCCG CTCGTGTAC GATGTTCCGA CCGTCGCCGC GAAACACGTC GACCGGGTCC

1101 AGGCCCTGCC TGAGAACGCT TCCCAGCAGA TCCATGCCCT CTCCTCCACC ACCCTGGATA ACATCCTGCA TGCCTTCTCT GAATCAGTG CTGCCCGTGT
TCCGGGACGG ACTCTTGCGA AGGTCTGTCT AGGTACGGAA GAGGAGGTGG TGGGACCTAT TGTAGACGT ACGCAAGAGA CTTAGTCAC GACGGGCACA

1201 GGTGGGAGGC TATCTGCTCA TGCTGSCCTA TGCTGCTGTG ACCATGCTGC GGTGGGACTG CGCCCACTCC CAGGTTCCG TGGCCTTGC CGGGTACTG
CCACCCCTCC ATAGACGAGT ACGACCGGAT ACGGACACAC TGGTACGACG CCACCCCTGAC GCGGTTCAGG GTCCCAAGGC ACCCGAAGC GCGCCATGAC

1301 CTGGTGGCCC TGGCGGTGGC CTCAGGCCCT GGGCTCTGTG CCTGCTCTGG CATCACCTTC AATGCTGCCA CTACCCAGGT GCTGCCCTTC TTGGCTCTGG
GACCACCGG ACCGCCACCG GAGTCCGGAA CCGGAGACAC GGGACGAGCC GTAGTGGAG TTACGACGT GATGGGTCCA CGACGGGAG AACCGAGAC

1401 GAATCGGCGT GGATGACGTA TTCTGTCTGG CGCATGCCCT CACAGAGGT CTGCCCTGGA CCCCTCTCCA GGAGCGCATG GCGAGTGTG TGCAGCGCAC
CTTAGCCGCA CCTACTGCAT AAGGACGACC CGTACTCGAA GTGTCTCCGA GACGGACCGT GGGGAGAGGT CCTCGGTAC CCGCTCACAG ACGTCCGCTG

1501 GGGACACAGT GTCGTACTCA CATCCATCAA CAACATGGCC GCCTTCTCA TGGCTGCCCT CGTTCCTATC CTTGCCCTCTC CTTACAGCCA
CCCGTGGTCA CAGCATGAGT GTAGGTAGTT GTTGTACCG CGGAAGGAGT ACCGACGGGA GCAAGGTAG GGACCGGAC CTCGGAAGAG GAATGTCGCT

1601 TCCTCAGCCT GGACCTACGG CGGCGCCACT GCCAGCGCT TGATGTCTC TGCTGCTTCT CCAGTCCCTG CTCTGCTCAG GTGATTCAGA TCCTGCCCCA
AGGAGTCGGA CCTGGATGCC GCGCGGTGA CGGTCCGGA ACTACAGAG ACGACGAAGA GGTACGGAC GAGACGAGTC CACTAAGTCT AGGACGGGCT

1701 GGAGCTGGG GACGGGACAG TACCAGTGGG CATTGCCAC CTCACTGCCA CAGTTCAAGC CTTTACCCAC TGTGAAGCCA GCAGCCAGCA TGTGTCACC
CCTCGACCCC CTGCCCTGTC ATGCTCACC GTACCGGTG GAGTGACGT GTCAAGTTG GAAATGGTG AACTTCGCT CACTTCGCT ACACCAAGTG

1801 ATCCTGCCCT CCAAGCCCA CCTGGTGCC CCACCTTCTG ACCCACTGGG CTCTGAGCTC TTCAGCCCTG GAGGTCAC ACAGGACCTT CTAGGCCAGG
TAGGACGGAG GGGTTCGGT GGACCACGG GGTGGAGAC TGGGTGACCC GAGACTCGAG AAGTCGGAC CTCCAGGTG TGCCCTGGAA GATCCGGTCC

1901 AGGAGGAGAC AAGCAGAAAG GCAGCTGCA AGTCCCTGCC CTGTGCCCGC TGGATCTTG CCCGAAATTC CTGCAGCCCG GGGGATCCAC
TCCTCTCTG TTCCGCTTC CGTCGACGT TCAGGACGG GACACGGCG ACCTAGAAC GGGTAAAGG GGGCCTTAAG GACGTCGGG CCCCTAGGTG

2001 TAGTTCTAGA GCGGCCGCCA CCGCGGTGGA GCTCCAGCTT TTGTTCCCTT TAGTGAGGT TAATTGCGG CTTGGGTATC TT
ATCAGATCT CGCGGCGGT GCGGCCACCT CGAGTCTGAA AACAAAGGAA ATCACTCCCA ATTAACGCG GAACCCATAG AA

FIG. 11B

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☒ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**

☐ **SKEWED/SLANTED IMAGES**

☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**

☐ **GRAY SCALE DOCUMENTS**

☐ **LINES OR MARKS ON ORIGINAL DOCUMENT**

☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**

☐ **OTHER:** _____

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